UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK
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ENDO PHARMACEUTICALS, INC.
and GRUNENTHAL GMBH,

Plaintiffs,

v. 12 Cv. 8060 (TPG)

TEVA PHARMACEUTICALS USA, INC.,
and BARR LABORATORIES, INC.,

Defendants.

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New York, N.Y.
March 27, 2015
11:40 a.m.

Before:

HON. THOMAS P. GRIESA

District Judge

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(In open court)

THE COURT: Let's resume with this witness.

MR. RHOAD: Good morning, your Honor. We wanted to let your Honor know that there was a scheduling issue with one of the defendants' witnesses. So what our plan was for this morning is that I would continue my examination of Dr. Fassihi, to get to a convenient breaking point hopefully in maybe 45 minutes or so. At that point we would be willing -- reluctantly, but we would be willing to stop our examination to allow the defendants to present a witness, Dr. Deer, who needed to testify today. He will hopefully starting before the lunch break and continue after the lunch break, and then we could finish him, and if there's more time, I will resume my examination of Dr. Fassihi, if that's okay with your Honor.

THE COURT: Of course it's okay.

MR. RHOAD: Okay. So just to reorient ourselves, your Honor, yesterday Dr. Fassihi went through the background of the technology and explained how drugs are released -- have to be released in the body, absorbed into the bodily issues, go through the liver, get into the bloodstream in order for them to become therapeutically effective. He talked about the dissolution curve and dissolution equipment and how that is drawn, as well as the pharmacokinetic curve or PK curve that reflects how much of the drug actually gets absorbed into the body.

Then he talked about, if you look at these slides as he went through the patent about the problem of chronic pain, that there were some oxymorphone formulations that were on the market in terms of an injectable product and suppository, and that the patentees believed there was a need for a controlled release oxymorphone.

And so let me continue with that point. I think that's where we are.

THE COURT: Go right ahead.

REZA FASSIHI, (Continued)

called as a witness by the Plaintiffs,

having been duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. RHOAD:

Q. Do you understand that when we're talking about patents and we're talking about claimed inventions that the claimed invention is what is in the claims of the patent that come at the end of the patent?

A. That's correct, yes.

Q. So the patent -- the claims at the end are what define the claimed invention?

A. Yes.

Q. And so we'll get into the specifics of some of the claims and the claim limitations in a minute, but can you describe for the Court at a high level what the nature of the claimed

inventions are that are taught and claimed in the '122 and the '216 patents?

A. Sure. As I have shown on this slide, '122 and '216 patents, they have claims that relate to controlled release oxymorphone formulation that would achieve specified dissolution and pharmacokinetic parameters which I went over also yesterday. This was discovered by Endo, and it was safe and effective, and it provided twelve hours of pain relief.

Q. And so let's look at a couple of representative --

THE COURT: Can I read this another minute?

MR. RHOAD: Sure.

(Pause)

THE COURT: Go ahead.

Q. So Dr. Fassihi, let's look at a couple of representative claims and walk through them limitation by limitation so we can see what exactly the claims are directed to. And let's start with claim 19 of the '122 patent. Okay?

A. Yes.

Q. If you could walk us through that claim, please.

THE COURT: Let me get that.

MR. RHOAD: It will be up on your screen, your Honor, if you would like to look at that, which may be more convenient because we highlighted particular sections.

THE COURT: Sure.

A. On this slide, claim 19 of '122 patent, it talks about an

analgesically effective controlled release pharmaceutical composition with a twelve-hour dosing interval in the form of a tablet.

Q. And just to review, analgesically effective, what does that manner?

A. That means it would relieve pain with a dosing interval that is mentioned here every twelve hours after administration.

Q. Let's go to the next limitation in claim 19.

A. The limitation -- another limitation of claim 19 is that it talks about oxymorphone pharmaceutically -- oxymorphone or pharmaceutically accepted salt of oxymorphone. That would be a sole active ingredient.

THE COURT: I want to interrupt and get better acquainted with the patent. So claim 19 is where in the patent, what column?

MR. RHOAD: 26, your Honor.

THE COURT: All right. Go ahead.

MR. RHOAD: Do you want to us go back and start over again?

THE COURT: I would appreciate that.

Q. Dr. Fassihi, can you start at the beginning of claim 19 again and start to walk us through each limitation.

A. Sure. The first limitation of claim 19 is that claim 19 talks about an analgesically effective controlled release pharmaceutical composition with a twelve-hour dosing interval

in the form of a tablet.
Q. And as you just explained to us, analgesically effective means it's effective in relieving pain, is that right?
A. That's correct.
Q. And a controlled release pharmaceutical composition, those are the controlled release dosage forms you were explaining to us about yesterday?
A. That's correct.
Q. And this is one that has a twelve-hour dosing interval?
A. That is right. So if we move to the next slide, another limitation of the claim is that the active -- it is an oxymorphone or salt of oxymorphone.
Q. Let me stop you there. It says a salt of oxymorphone. Is oxymorphone hydrochloride a pharmaceutically acceptable salt of oxymorphone?
A. That is correct, yes.
Q. And in fact in all the tablets, what is the active ingredient in those tablets?
A. Oxymorphone hydrochloride.
THE COURT: Let me look at this another minute.
MR. RHOAD: Sure.
THE COURT: Go ahead.
THE WITNESS: Shall I go over this, your Honor, or the next slide?
Q. Why don't you -- so you started this limitation we have on

the screen on PX 4002.54, and you said it had to have oxymorphone or pharmaceutically acceptable salt thereof, and if you continue from that point.

A. That is the sole active ingredient in the tablet, and it is a controlled release delivery system. It is comprising hydrophilic material that forms a gel upon exposure to gastrointestinal fluid.

Q. So is that -- it says controlled release delivery system, is that the thing that provides the controlled release of the dosage form?

A. That is correct.

Q. And the hydrophilic material that forms a gel, is that one of the examples of a controlled release dosage form that you discussed yesterday?

A. That is right, yes.

Q. And if we could go maybe to that slide, slide 12.

A. So this is a slide that I showed yesterday. So a controlled release tablet that makes a gel is described here on this slide. So there is a tablet at zero hours, and then in the aqueous environment of the gastrointestinal tract it hydrates, swells, as you can see in two hours, four hours, eight hours, and it starts degrading and releasing drugs continuously, and by twelve hours nothing of this system is left.

Q. Let's go back then to where we were in the claim

limitation.

A. Sure. So another limitation -- so this is a gel forming that we talked about, if you go to next slide.

Another limitation of claim 19 relates to specifics of dissolution testing. And I showed on slides yesterday how dissolution care is obtained, and condition of that dissolution is described here, USP paddle method.

THE COURT: I'm not understanding you now. Take it a little slower.

Q. Maybe if we could go to back to slide 20.

A. So your Honor, one of the limitations relates to dissolution studies, and this is an apparatus that I was talking yesterday that put the tablet into these vessels, which are blue in color and they have medium in them, the paddle which is inside rotates.

Then go to the next slide where dissolution curve is there. So this is a dissolution curve that we are talking about. So the tablet releases the drug, we measure it, and then we plot it in this manner, the curve, and this is called dissolution curve. So the specifics of obtaining this dissolution curve are in the limitations of the claims.

So if you go back to the slide 19 on the limitations, please.

Q. If we could go back for one moment to -- this is slide 21. Is the paddle that is referred to in the claim the type of

equipment that is shown on the left here?
A. That is correct, yes.
Q. So let's go back to the slide that has the limitation, please.
A. So your Honor, this first part of the limitation is what I described just now. So it talks about in vitro dissolution test, it talks about USP paddle method, and 50 RPMs, the rotation of the paddle.
Q. What does RPM mean?
A. It means revolutions per minute, so number of times that it revolves, the paddle rotates in one minute.

Then it talks about that media, the aqueous environment, 500 milliliter. And there is also a pH -- range of pH that the tablet would be tested in one of those pHs.
Q. And then the second part of the limitation --

THE COURT: I'm really not getting this.

THE WITNESS: So shall I go over it one more time, your Honor?

THE COURT: I think you better do that.

THE WITNESS: Sure. So it says whereupon placement of the composition. So this is a controlled release composition that we talked about the hydrophilic matrix.

THE COURT: If you could pause.

Why are you suddenly focusing on claim 19?

MR. RHOAD: Your Honor, we wanted to walk your Honor

through one of the claims -- there is some overlap in the types of limitations that are -- the limitations that are described in the different claims. So we just picked one that would -- that we were hoping would try to illustrate some of the limitations that you will see in other claims as well.

This is one of the claims that we are asserting that each of the defendants infringes, so we are claiming that they infringed this particular claim. And so what we were planning to do was go through this claim as well as claim 20, which has some other limitations that are not found in this, and then also talk about some limitations that aren't either one of those two claims but are in other claims so your Honor would get a feel for the concepts, what the limitations are about, so that as you are reading the patent and reading all the different claims, hopefully you would have a background in what they were talking about.

THE COURT: Now I have to tell you that I have tried patent cases before, but by mutual consent between me and the lawyers, we used very untechnical terminology.

What is a limitation?

MR. RHOAD: A limitation, your Honor, is a part of the claim. So under the law, the law says to prove infringement you have to compare the claim against the product, and everything that is recited in the claim has to be found in the accused product. And the lawyers refer to limitations meaning

different parts of the claim. So if we look at the first slide --

THE COURT: That's all I need.

MR. RHOAD: Sorry, your Honor. So limitation just refers to a particular part of the claim. So maybe I could show you on a slide we have. Looks like 86, please.

So your Honor, here we have on slide 86, this is claim 19 of the '122 patent, and all of the words of the claim are here on the slide. And what we have done is kind of broken it down piece by piece so that you can compare each piece and see does the accused product include each of these pieces. And we patent lawyers refer to those individual pieces as limitations, so it's sort of a part of the claim.

THE COURT: Okay. Fair enough. Go right ahead with your questioning.

MR. RHOAD: Your Honor, we're on slide 55, and as Dr. Fassihi just explained, it says wherein upon placement of the composition, and so when it's referring to the composition, it's talking about that extended -- that controlled release oxymorphone tablet that was recited earlier on in the claim where we saw up here at the beginning of 19 it says an analgesically effective controlled release pharmaceutical composition with a twelve-hour dosing interval in the form of a tablet.

So then when we get later on in the claim and it says

wherein upon placement of the composition, it's referring to that tablet, in an in vitro dissolution test. So in vitro, Dr. Fassihi explained earlier, means in the laboratory. So this is a dissolution test in the laboratory using that equipment that he showed us earlier with the paddle. And it says that test in particular is something, USP paddle method.

BY MR. RHOAD:

Q. So Dr. Fassihi, can you explain what USP paddle method is?

A. Yes. What I showed in the previous slide with the schematics picture of apparatus, that was USP paddle method.

THE COURT: Wait, just a little louder and a little slower, if you could.

THE WITNESS: Sure. So USP paddle method was the one that I showed the picture of that in the previous slide.

Q. First of all what, is USP?

A. USP, your Honor, is United States Pharmacopeia, which is a standard book that formulation pharmacists and scientists use for understanding certain methodologies and things like that. So this is a method which is described in the United States Pharmacopeia, which is a standard book that we use in the development of pharmaceuticals.

Q. And if we could go to slide 20, please.

Is this a picture of equipment that you could use to perform the USP paddle method dissolution test?

A. That is correct. So this is a United States Pharmacopeia

named dissolution apparatus called paddle -- well, this one is just a dissolution apparatus.

Q. If we go to the next page, slide 21, on the left-hand side we have a picture of the paddle?

A. That's correct.

Q. When it says USP paddle method, it means you're using dissolution testing that has this type of paddle?

A. That is correct, yes.

Q. And the claim, when it refers to 500 ML media, is that referring to the amount of the blue liquid we see on side 20?

A. That is right, yes.

Q. And when it refers to 500 RPM or revolutions per minute --

A. 50.

Q. Sorry, 50 RPMs, does that mean that that paddle is spinning around at 50 times every minute?

A. That is correct, yes.

MR. RHOAD: So here, your Honor, we're back at that claim limitation in claim 19. So I think he has just explained that first part about in vitro dissolution test comprising USP paddle method, so using equipment that includes the paddle, at 50 RPM, or that paddle is spinning around 50 times every minute, in 500 ML media, so that blue liquid, there's 500 milliliters of that blue liquid. And that has a particular pH.

BY MR. RHOAD:

Q. And what is pH?

A. PH is the measurement of either acidity or acid character of the solution in this case. So pH 1.2 is acidic, up to 6.8, which is more or less neutral. That so that is a range of pH which is similar to the pH in the GI tract in our body.

Q. And it specified a particular temperature.

THE COURT: We have had it before. What does pH mean? Can you tell me again?

THE WITNESS: Sure. So the pH, your Honor, is the measurement of if a liquid is acidic or, for example, if you have a glass of water and we squeeze some lemon in it, it becomes acidic. And the reason for that is because in the human body in the stomach we have acidic conditions. So the dosage form that we swallow, it goes into the acidic environment first. So we are trying to mimic something like that in this test.

BY MR. RHOAD:

Q. And that is at a particular temperature, 37 degrees Celsius?

A. That is right. That is similar to body temperature.

Q. So to sum this up, what this limitation is saying is that you have to run an in vitro dissolution test, a test in the lab of the dissolution, and you have to do it using this particular method and these particular conditions, is that right?

A. That is correct, yes.

THE COURT: I have got to test your patience. Explain

again what is meant by pH of 1.2 to 6.8. Go over that again.

THE WITNESS: Sure, your Honor. In this apparatus we have 500 milliliters of a media, as it is shown here. That media could have a pH -- in other words, that media could be acidic, and the measurement of that acidic character is measured by a piece of apparatus called pH meter. So we measure that. And pH is important because we like to know --

THE COURT: PH means the degree of acid?

THE WITNESS: That is right, yes.

THE COURT: Okay.

BY MR. RHOAD:

Q. And does a lower pH mean more acidic, more acid?

A. That is right, your Honor. 1.2 is a strong acidic condition, and 6.8 is kind of neutral, it's like water. A glass of water is neutral. So when we talk about pH of 6.8, maybe a glass of water has a pH of 6.8 or 7, but then when we come down to 3, 2, 1, it becomes more acidic.

Q. So then the claim limitations or the claim goes on, and so it's when you do a test, a dissolution test in the lab with those particular conditions, then where does the claim go from there?

A. So the second part of the claim, that limitation in the box below, talks about how much of the drug is released when we do the dissolution, every, for example, in time point. So 15 percent to about 50 percent of the drug is released in one

hour, and that is highlighted in yellow, your Honor, for convenience. So 15 percent to about 50 percent of the drug comes out of the dosage form in about one hour.

THE COURT: Just a minute.

I see.

A. And by the same measure, if we move further in dissolution testing, we see that they show 45 percent to about 80 percent of the drug is released at about four hours, which is also highlighted in yellow.

THE COURT: Okay.

A. Then it goes on to say at least about 80 percent of the drug is released at about ten hours, which is also highlighted for you.

Q. So this is referring to the dissolution curve and the particular dissolution results that you get --

A. That is correct.

Q. -- from doing the test.

If we go to the next slide, can you explain what you were showing here?

A. Sure. So your Honor, in this slide all those percentages which were in the limitations are highlighted here. So the first red bar to the left has a range. The lowest part is about 15 percent and the highest part maxes at 50 percent. So that is our range for one hour. At four hours, as the limitation indicated, the lowest point is 45 percent and the

highest point is 80 percent. And at ten hours at least 80 percent should have been released, and we just have that lowest that is 80 percent, and it can maximum go to 100 percent. We cannot go beyond that.

(Continued on next page)

Q. All right, maybe if we can go back to slide 22, and this was the dissolution curve that you explained earlier, is that right?
A. That is right.
Q. So using that dissolution curve apparatus, you would take various measurements at different time points?
A. That is correct.
Q. Then you would draw a line through those time points to get your curve?
A. That is right, yes.
Q. And so then if we can then go back to slide 56, so, in other words, you had these red bars here, in order to meet those limitations, that curve that we just drew would have to go between these red bars, is that right?
A. That is correct, yes. If it goes through the red bars, that means the limitations are met.
MR. RHOAD: Okay, your Honor, so we have gotten all the way through claim 19.
THE COURT: Let me look at this once more.
(Pause)
THE COURT: Look, I am sure it is somewhere relevant, but I don't see some of this in the words of claim 19. For instance, I don't see in claim 19 anything about 15 percent being dissolved. Wait a minute. I am not reading it right.

MR. RHOAD: Claim 19 continues on to the next page, into column 27, so that appears on the next page. That claim happens to be split across the page.

THE COURT: You mean I have to turn a page? You are very demanding. Let me look at it now, please.

Oh, of course, I see it. All right. Very good. You can go ahead.

MR. RHOAD: Okay, your Honor. So that's claim 19 of the '122 patent. So the other claim, we went on a run through two identical claims, so the next claim is claim 20, the very next claim of the '122 patent, so that is in column 28 is where it starts. Do you see that, your Honor?

THE COURT: I am going to bother you for a minute. I want to look a little more at claim 19.

MR. RHOAD: Certainly.

THE COURT: Give me a minute.

MR. RHOAD: Your Honor, I have claim 19 written out sort of limitation by limitation that I can hand up a hard copy of or we can look at a particular place on the slide deck if that would help your Honor.

THE COURT: Actually what I want to do is to really begin to get acquainted with these claims as they are presented in the patent. I want to get acquainted with those claims as presented, as I am saying.

(Pause)

THE COURT: I think I have finished looking at claim 19 as much as I want to at the moment. Go ahead with what you want to ask the witness now.

MR. RHOAD: Your Honor, we want to move on to claim 20 of the '122 patent.

THE COURT: Okay.

MR. RHOAD: If it would be useful for your Honor, maybe we can hand up again the way we have broken it out, limitation by limitation, so that it might be a little bit easier to follow.

If we start with claim 20, do you have a set of the slides, your Honor?

THE COURT: I am sure I do.

MR. RHOAD: Your Honor, I just handed up to you slide 102.

If you can pull that up.

As I was mentioning before, this is kind of the claim 18 broken out piece by piece and claim 20. So if you look at the bottom of this page, do you see where it says "the method of claim 18"?

THE COURT: I do, of course.

MR. RHOAD: So what that means is, that is what lawyers call a dependent claim, and claim 18 is the independent claim. So in order to infringe claim 20, you would also have to have everything that's in claim 18. So we can start by

going back to claim 18 and then the first limitation there reads, "A method of treating pain in a subject in need thereof the method comprising."

THE COURT: I see.

MR. RHOAD: Your Honor, when we are talking about method claims, claim 19 was talking about pharmaceutical composition, so it's what we lawyers sometimes call a composition claim or a product claim, meaning the claim is to the product. A method claim is a method of performing certain steps, so this is that type of a claim is performing certain steps.

Q. Dr. Fassihi, looking at this first, can you explain, it is a method of treating pain and then it says "in a subject in need thereof." What is that referring to?

A. It is referring to a method today to treat pain, to relieve pain.

Q. And "in a subject in need thereof," that means somebody who needs to have their pain relieved?

A. That is right. It could be a patient and a method that comprises, and then it goes to the next limitation, which is administering to the subject the pharmaceutical composition of claim 1, in other words, that control release tablet would be administered to the patient.

MR. RHOAD: Your Honor, claim 1 is very similar to claim 19 that we just looked at in that it talks about an

analgesically effective controlled-release pharmaceutical compound, composition, so that is the one in the middle row there with a 12-hour dosing in the form of a tablet, so that is exactly what we just had in claim 19 that we just walked through. It says oxymorphone or pharmaceutically acceptable salt thereof as the sole active ingredient, and then it talks about a controlled-release delivery system comprising at least one pharmaceutical excipient, and then it talks about the particular dissolution method, and that only has one time point. So if we saw on claim 19, if you recall, there were three different time points -- one-hour, four-hour and ten-hour time points -- for the dissolution, this one just says 15 to 50 percent by weight in the last line of that middle column about one hour into the test. So that part is covering a tablet.

So if we go back to the second slide on the line, it says administering to the subject, to the person who needed to have pain relief, so somebody needs to be treated for their pain, you administer to that subject a pharmaceutical composition of claim 1 which is the tablet, the controlled-release oxymorphone tablet.

Are you with us?

THE COURT: Yes, I am.

MR. RHOAD: Then let's go to the fourth line, beginning "comprising about."

Q. Can you explain what that limitation is, Dr. Fassihi.

A. Sure.

So it talks about dosage form, which has about five milligrams or about eight milligram of oxymorphone or pharmaceutically acceptable salt thereof. So the dosage form comprises of that. So that talks about presence of active drug, which is oxymorphone.

Q. That is just telling us how much of the oxymorphone has to be in this tablet, is that right?

A. That is correct.

Q. So that is claim 18.

THE COURT: Wait a minute. Just a minute, please.

Okay. I see. Go ahead.

Q. So then we are done with claim 18, so claim 20 is the method of claim 18, so what we just talked about, and then it says "wherein, upon oral administration of the composition," so that's referring to giving that tablet to somebody, taking that orally through the mouth, is that right, Dr. Fassihi?

A. That is right.

Q. And then it says, "The oxymorphone AUC zero to infinity is no more than 20 percent higher when the composition is administered to the subject under fed conditions, as compared to fasted conditions."

So maybe at first we can reorient the court as to what that AUC parameter is. We talked about that yesterday.

MR. RHOAD: If we can go to slide 41, please.

So if you recall, your Honor, that is the slide that we used to explain to your Honor what the AUC or "area under the curve" is.

Q. Dr. Fassihi, do you want to reorient us as to what we are talking about here?

A. Sure. So this is an AUC that we talked about yesterday, and that is area under this curve, "AUC" stands for "area under the curve." So that is a representation of how much drug is in the blood circulation in the body of the human being after the dosage form is taken. So if I take a tablet, the drug would be absorbed from my GI tract and reaches blood circulation, and it shows the curve like this. This is called area under the curve, AUC, and it represents how much drug is there in my body.

MR. RHOAD: Then if we can go to slide 62, please.

So, your Honor, here on this slide we have blown up this limitation we are talking about, and it says "Where AUC zero to infinity" -- that area under the curve we were just talking about -- "is no more than 20 percent higher when the composition" -- when that controlled-release oxymorphone tablet -- "is administered to the subject under fed as compared to fasted conditions."

Q. So, Dr. Fassihi, can you explain to the judge what that's referring to under fed as compared to fasted conditions?

A. Sure. So basically it means here in this slide, your Honor

patient would sometimes take the tablet after they have had food, so here on this slide -- and that affects how much gets absorbed. So in this slide, there is a green bullet point which describes the patient took the tablet right after having eaten a meal. That is called fed conditions. That means I had a meal and then I took my tablet.

Alternatively, I can take it on an empty stomach. That means I have not ingested any food. That is referred to as fasted conditions.

It is important for dosage forms that we should know whether there is any difference in amount of drug that gets into the blood circulation when we take it with food or when we take it on a fasted, empty stomach. So that difference in blood levels is important and food can impact it, can increase it or maybe decrease it, we can see that.

Q. So when we were talking earlier about the four steps by which a drug in a controlled-release dosage form goes through to become effective, it first has to be released out of the dosage form, then it has to be absorbed into the body, is that right, in the second step?

A. That's correct.

Q. Whether or not there is food in your stomach and the intestines can effect that second step, how much gets absorbed into the body?

A. That is correct, yes.

Q. So let's try and explain this a little bit more maybe. Can you tell us what's shown here on slide 64.

A. Sure. So, your Honor, fed condition is we take the breakfast, like what is shown here, and more or less similar breakfast, you take that and ten minutes after ingesting the breakfast, you take your tablet.

And the other side, on the right-hand side, subjects or patients that are tested, they have dinner the night before and they take nothing. In the morning, when they take the tablet, there is no food in their stomach. They take the tablet.

We start collecting blood, blood samples from these subjects and we see if there is any difference between those individuals that ingested the meal and then they took the tablet and those that did not have breakfast and took the tablet. So we compare those two together, their blood levels.

THE COURT: All right.

A. So that is called fed condition and fasted condition.

Q. Okay. Is there any data provided in the patent about whether or not there is -- strike that. Let me back up a second.

Is that sometimes called "the food effect," the difference in blood levels in a patient between whether they have taken it with food, like after a meal, under fed conditions, or on an empty stomach, after fasted conditions?

A. Yes, it is often referred to as "food effect," yes.
Q. So they take those blood levels and they measure whether or not there is any difference between those two conditions, and that is the food effect?
A. That is correct, yes.
Q. Is there any data provided in the patent itself about whether or not the oxymorphone formulations that the patentees tested exhibited any difference between these conditions, any food effect?
A. Yes, there is.

Your Honor, here, is what is in the patent specification. So the upper box is column 19 of the patent, line 15 to 19.

MR. RHOAD: Your Honor, this is from PTX 001, which is the '122 patent, and we have blown up some language from column 19 of that patent.

THE COURT: Again, I am saying this over and over maybe, but I am trying to get acquainted with the patent. The slides are very helpful, but I want to get acquainted with this very important document. Where on the --

MR. RHOAD: We are in the '122 patent at column 19.

THE COURT: Where in column 19?

MR. RHOAD: Starts on line 15, so if you see -- do you see the line numbers?

THE COURT: I sure do.

MR. RHOAD: It is the sentence that begins "both rate and extent of," on that line.

THE COURT: All right. Very good. I see that. Go ahead with the testimony.

BY MR. RHOAD:

Q. So, Dr. Fassihi, could you just please read into the record the sentence we have highlighted on the slide?

A. Sure. So this is excerpt from '122 patent in column 19 and it reads, "Both rate and extent of oxymorphone absorption from the oxymorphone oral solution were affected by food," and then it talks about some technical terms like LS squared mean.

THE COURT: What are you saying now?

THE WITNESS: Your Honor this is technical term in the description here, which is not -- I point to --

BY MR. RHOAD:

Q. Maybe, Dr. Fassihi, it says "both rate and extent of oxymorphone absorption," so is that referring to that second step and third step that we are talking about, the rate and how much and how fast the oxymorphone is getting absorbed into the body, into the bloodstream?

A. That's correct. So "rate" means how fast and "extent" means really representation of AUC.

Q. And when it refers to oxymorphone oral solution, does that mean not like the tablets that are part of the claimed invention, but somebody took a solution, some liquid that had

oxymorphone in it and drank it?
A. That is correct, because the idea here was to check the food effect by giving solution of oxymorphone so that it is rapidly absorbed with food and also controlled release with food. And in the first part that we went over just now, let's focus on the AUC, since we talked about that, so it talks about AUC that basically increased approximately about 30 percent -- and that is the wording in the patent -- 30 percent increase when solution was taken with food.
Q. So when we are talking about the oral solution, we are talking about an immediate-release formulation, is that right?
A. That is correct, yes.
MR. RHOAD: So, your Honor, you may recall yesterday Dr. Fassihi explained immediate-release formulations versus controlled-release formulations. And because this is a solution, there is no tablet for the oxymorphone to dissolve out of, so it is immediately available. It is an immediate-release formulation and is this indicating, Dr. Fassihi, that for an immediate-release oxymorphone that they tested, the area under the curve, the amount of drug absorbed increased about 30 percent when it was taken under fed conditions, so after a meal, versus when it was under fasted conditions, basically on an empty stomach?
THE COURT: Ask your question again. It's got a lot of parts to it.

Q. In this paragraph or this excerpt we are talking about an immediate-release oxymorphone formulation. Is that correct, Dr. Fassihi?
A. That's correct, yes.
Q. It is explaining that and it is talking about the effect that the presence of food had on the area under the curve, AUC. Is that right?
A. Yes.
Q. And the area under the curve, you explained, is the total amount of the oxymorphone that gets absorbed into the bloodstream, is that right?
A. That is correct.
Q. It is explaining that for that immediate-release oxymorphone formulation, the amount of drug absorbed was 30 percent higher when it was taken with a meal as compared to the total amount that got absorbed --
A. Without meal.
Q. -- without a meal, is that right?
A. Yes, that's right. So this was a food effect, your Honor. The area under the curve, which is amount, total amount absorbed when they gave oral solution, it increased when food was taken by 30 percent.
THE COURT: I understand.
A. So that is the essence of that excerpt.
Q. On the next, below that, we have excerpts from, again, the

'122 patent, column 19, beginning from lines 9 to 13. Okay? Is that talking about the same thing, the same difference in the extent of oxymorphone absorbed, the AUC, except talking about a controlled-release formulation?

A. That is right. So this section talks about giving controlled-release oxymorphone tablet and when patients were taking food. So food increased the AUC by about less than 20 percent.

Q. So, whereas, for immediate release, the presence of food increased the AUC by 30 percent.

A. That's correct.

Q. For a controlled-release formulation of oxymorphone, the AUC, or drug absorbed, was less than 20 percent, is that right?

A. That is right.

Q. And, in general, is it a good thing or a bad thing to have a lower AUC? So here we saw that the controlled release difference in the food effect for a controlled-release formulation was lower and less than 20 percent, is that generally a good thing or a bad thing from the manufacturer's perspective?

A. It is a good thing in many ways. That means if I take controlled-release formulation today now --

THE COURT: That means what? Say it again with.

THE WITNESS: That means if I take the oxymorphone controlled-release tablet, with food or without food, I am

assured that the AUC, the extent of absorption, is not more than 20 percent different. In other words, increases with food, increases in AUC with food or fasted is less than 20 percent.

THE COURT: And why is that good or bad?

THE WITNESS: It is good, your Honor, because oxymorphone controlled-release formulation is to be taken --

THE COURT: Because of what? Say it again.

THE WITNESS: Because oxymorphone controlled-release formulation, the tablet, is to be taken every 12 hours; and during the day we consume food. We take breakfast, lunch, and dinner. So there is always food in our body, in our stomach. And when we take the tablet, if the AUC is low, variation in AUC is low, it is a good thing because in a predictable manner I can take the medication and be assured that my blood levels are not very high, the extent of drug in my body is always controlled and low. So the low AUC is good. Low AUC with food and without food is good because the percentage in AUC are not too far apart. So let me explain it more.

THE COURT: I have to bother you to explain why is it good or bad --

THE WITNESS: Sure.

THE COURT: -- once more.

THE WITNESS: Sure.

So I would like to take a tablet that doesn't show too

much variation in its total absorption into my body when I take food and when I am taking it on an empty stomach.

THE COURT: I see what you mean, okay.

THE WITNESS: So it is a good thing that can happen, that.

Q. So is that data that was in the patent showing a less than 20 percent difference in the AUC values between these two conditions, is that reflected in the claim limitation?

A. Yes, it is. So in the claim actually talks about less than 20 percent difference in AUC values under fed versus fasted. So that means that if the tablet was taken on a stomach that had food in it and was fasted, empty, the difference is less than 20 percent.

THE COURT: Let's take a recess, please.

MR. RHOAD: Okay.

(Recess)

MR. RHOAD: Your Honor, we only have a limited time before the lunch break, so what I wanted to do was to go over -- I am actually pleased to report that the parties have agreed to a stipulation regarding some of the facts in this case that will help further narrow some of the issues, and some of them relate to infringement issues, so we have it all signed and I will hand it up to your Honor maybe right before the lunch break or I can do it --

THE COURT: Whenever it is convenient for you. You do

what is convenient for you.

MR. RHOAD: So I wanted to put here on the Elmo. If we can maybe zoom in a little bit.

So there are two parts to the stipulation. One relates to the infringement issues. Those are the ones I will highlight for your Honor right now. There are some that relate more to validity issues, and they are in the stipulation that has been signed, but I won't go through them with your Honor. But what it says here is that "each defendant stipulates that its accused tablets" -- so Dr. Fassihi hasn't explained exactly what those are, but those are the tablets that are the subject of the defendant's abbreviated new drug applications -- "satisfies each limitation of each '122 and '216 patent claim asserted against them, as set forth in Exhibit A, except that defendants dispute" three sets of issues, and they are specified in paragraphs one, two, and three.

THE COURT: Just pause for a minute and let me look at that, please.

MR. RHOAD: Absolutely.

THE COURT: What is Exhibit A?

MR. RHOAD: Exhibit A is Exhibit A to this stipulation, which is a list of each claim that the plaintiffs are asserting in this case against each defendant. So if we see here, your Honor, on the left-hand side we have a list of the defendants and there the accused products, the first one

there is Actavis CRF, then case number in parentheses, so your Honor knows what that case number is. So two of the defendants have filed two ANDAs, so Actavis and Ranbaxy have filed two ANDAs, so they are listed here twice.

THE COURT: Just a second. Give me that name again.

MR. RHOAD: Actavis is the first one listed there.

THE COURT: Filed what?

MR. RHOAD: The very first row of the -- oh, they filed an ANDA, abbreviated new drug application, seeking to sell --

THE COURT: Wait a minute. A-N --

MR. RHOAD: -- D-A.

THE COURT: And that --

MR. RHOAD: That stands for abbreviated new drug application.

THE COURT: Go back to where you were.

MR. RHOAD: Sure.

So each of the defendants in this case has filed an abbreviated new drug application, and they are essentially seeking the FDA's approval to get on the market with a controlled-release oxymorphone formulation that is a generic version of Endo's Opana ER product that you heard Dr. Lee talk about yesterday and the past few days. So each one of these we have, these are all the cases that are before your Honor as part of this trial.

And so the first one there, Actavis CRF, that's their crush-resistent formulation, that is the ANDA they filed seeking approval to market a generic version of Endo's crush-resistent formulation of Opana ER.

And then, as you move over one column over, you see at the top it says "'122 patent claims" in the blue? It is a little fuzzy on the Elmo. Do you see that? Where I am pointing my finger, '122 patent claims. Let me hand up the signed version. That might help your Honor.

THE COURT: It might. On the screen that just doesn't show up at all.

It amazes me why you would put dark green ink on a dark green background.

MR. RHOAD: I wasn't the one who did that, your Honor.

THE COURT: What are the headings? I will write them out.

MR. RHOAD: The column on the left is "Defendant." The second column over says "'122 patent claims."

THE COURT: In other words, claim 2, claim 3, claim 19 --

MR. RHOAD: That's exactly right, your Honor.

And the last column on the right is "'216 patent claims."

THE COURT: Okay. Very good. Very good.

BY MR. RHOAD:

Q. So what is shown on the chart in each row, each row relates to a different abbreviated new drug application filed by one of the defendants, so in the first row it refers to the abbreviated new drug application filed by defendant Actavis, and the CRF indicates that it relates to -- it is as ANDA directed to Endo's crush-resistent formulation of Opana ER.

THE COURT: Just a minute. So CRF --

MR. RHOAD: -- stands for crush-resistent formulation.

THE COURT: Okay.

MR. RHOAD: So what this means, then, is that Endo is asserting claims for and that Actavis CRF product infringes claims 2, 3, 19, and 20 of the '122 patent. Do you see that?

THE COURT: So, in other words, that in the second column for Actavis has 2, 3, 19 and 20, these are the claims allegedly infringed, right?

MR. RHOAD: That is correct, your Honor.

THE COURT: And is the same thing true of the --

MR. RHOAD: -- '216 column, that's exactly right, your Honor.

THE COURT: Okay. Very good.

MR. RHOAD: So then if we can go back to the portion of the stipulation that I had on the screen earlier, which we can --

THE COURT: Can I interrupt you?

MR. RHOAD: Certainly.

THE COURT: Now, 1:00, I know you have some scheduling things about a witness or two. I would normally recess now until 2:15, but what I am asking is, is there something you want to finish, anybody wants to finish --

MR. RHOAD: What I was hoping to finish, your Honor, is that there are a number of claims that I have highlighted here in which, based upon the stipulation, the defendants do not dispute and have stipulated that they satisfy each piece of these asserted claims. And I was just going to ask Dr. Fassihi if, in light of that, he has an opinion whether they infringe, and that was where I was hoping to end, and then we could break for lunch.

THE COURT: Very good. That's very good.

MR. RHOAD: So, your Honor, just very quickly, here on the page of the stipulation that's on the screen it says, "Each defendant stipulates that its accused tablets satisfy each limitation of each '122 and '216 claim asserted against them as set forth in Exhibit A." So they are saying that, for each of those claims we were just looking at, that are listed as the allegedly infringed claims, they are stipulating that their tablets satisfy each piece of those claims, except as they relate to the three paragraphs that are specified there. And we will talk about those three paragraphs and what those issues are more later.

And then it also says below that that "Endo need not

present any proof of infringement at trial that the defendants' accused tablets satisfy any claim limitation not in dispute as recited above." So it is saying, basically, other than those three categories of issues, we don't have to put on proof of infringement, we don't have to prove their tablets meet each piece of each claim unless it is encompassed within one of those three paragraphs. Okay? Are you with me?

THE COURT: Certainly.

MR. RHOAD: And those three paragraphs specify which particular claims have issues that are in dispute, and I will represent to you, your Honor, that I have here highlighted the fact that my understanding is -- and I invite any defendants' counsel to stand up now or forever hold their peace -- that those three issues do not implicate any of the '122 patent claims 2, 3, or 19.

THE COURT: Wait. I don't know what you are saying.

MR. RHOAD: So with respect to claims 2, 3, and 19 of the '122 patent, pursuant to this stipulation, defendants have stipulated that their tablets satisfy each limitation of those claims, in other words, they satisfy each piece of each of those claims and the standard for infringement is if you satisfy each piece of each claim, you infringe.

THE COURT: 2, 3 and 19. You leave out 20.

MR. RHOAD: So that is a claim that is in dispute. That is a claim that has limitations, has pieces that are going

to be in dispute. So we will have to put on evidence of that.

But as to 2, 3, and 19, pursuant to this stipulation, we don't have to put in evidence that they satisfy those limitations because they are stipulating that, with respect to all of those claims, there is no dispute about any of the proofs that we would have put on. So they are stipulating --

THE COURT: Where does the stipulation say what you just said?

MR. RHOAD: If you go back in the two highlighted sections that we have here, it says they stipulate that the accused tablets, so each one of their accused tablets, satisfies each limitation or each piece of each '122 and '216 patent claim asserted against them as set forth in Exhibit A -- so that's the exhibit we were just looking at, that chart -- except that they dispute these three categories of issues, disputes.

So if we look, for example, at the first paragraph, it says they dispute that their accused tablets satisfy the AUC and C max food effect limitations recited in the '122, claim 20 and '216 claims 40, 42, 50, 54, 78, 79, 80, and 82. So, in other words, that's that limitation that we were just looking at the very end, the AUC food effect difference, fed versus fasted. So there they are disputing one of the pieces of '122, claim 20. So that's why I didn't identify that as a claim that is not disputed.

THE COURT: I understand.

MR. RHOAD: So what I am telling you is these three sections identify which claims and which limitations are at issue, and claims 2, 3, and 19 are not within the scope of any of those disputed issues. So there is no dispute in this case that each of the defendants' tablets all satisfy all limitations of claims 2, 3, and 19 of the '122 patent.

THE COURT: Very good.

MR. RHOAD: Then, similarly, it is my belief -- and I invite, again, any defendant to stand up or forever hold their peace -- that of the '216, claims 1, 22, 73 and 74 are not implicated by any of those disputed issues, so that there is no dispute and it is stipulated that each of defendants' tablets satisfy each limitation of those claims.

THE COURT: Okay. Very good.

BY MR. RHOAD:

Q. Dr. Fassihi, in light of your understanding of the legal standard for proving infringement and the stipulation that the defendants' tablets satisfy each limitation of claims 2, 3, and 19 of the '122 patent and claims 1, 22, 73, and 74 of the '216 patent, to the extent shown here on Exhibit A, do you have an opinion as to whether or not each of those tablets infringes the claims I just identified?

A. Yes.

Q. And what is your opinion?

A. They all infringe these patents '122 and '216 and the claims that were mentioned.

MR. RHOAD: With that, your Honor, I think we can take a break for lunch.

THE COURT: Are we ready to resume at 2:15?

MR. BLACK: Yes, your Honor, with a different witness.

THE COURT: Okay. Very good. 2:15.

(Luncheon recess)

AFTERNOON SESSION

(2:20 p.m.)

THE COURT: Who is the witness now, please?

MS. CRUZ: Good afternoon, your Honor, my name is Carol Pitzel Cruz with Knobbe Martens on behalf of the defendants. And Dr. Deer is the witness, if we could call him up to stand.

THE COURT: All right, we'll have him.

TIMOTHY RAY DEER,

called as a witness by the Defendants,

having been duly sworn, testified as follows:

DIRECT EXAMINATION

BY MS. CRUZ:

DEPUTY CLERK: Speaking into the microphone, would you state your full name for the record and spell your first and last name.

THE WITNESS: Timothy Ray Deer, T-I-M-O-T-H-Y, R-A-Y, D-E-E-R.

MS. CRUZ: Your Honor, since we are taking Dr. Deer out of order, I want to give a little context that he is a medical doctor, and we will go through this him in more detail.

THE COURT: All right now, very good.

MS. CRUZ: And so Dr. Deer is going to testify to two issues in the case, one will be the use of Ranbaxy --

THE COURT: Your name again, please?

MS. CRUZ: Carol Pitzel Cruz.

THE COURT: Very good.

MS. CRUZ: And so one of those issues will be how patients will use Ranbaxy and Roxane's products, and if that use satisfies several pieces of some of the claims that Mr. Rhoad had gone over earlier today, and we'll highlight those issues.

And then there's also a few issues that Dr. Deer will respond to that plaintiffs have raised or will raise in the case regarding the use of Opana ER as well as other opioids from the doctor's perspective.

BY MS. CRUZ:

Q. Dr. Deer, have you prepared a set of slides to help with your presentation today?

A. Yes, ma'am, I have.

MS. CRUZ: Your Honor, do you have a set of the slides up on your desk with you?

THE COURT: Very good.

Q. So if we could turn to slide two. Also in your binder there should be a tab marked DX 6000.

A. Yes, ma'am, I have that before me.

Q. Can you tell us what that is?

A. Yes, that's my curriculum vitae.

Q. Is that accurate?

A. I believe it is, yes.

Q. If we could look at the sides, we could run through some points on your career and expertise.

So if you could describe generally your current position at the Center for Pain Relief.

A. Yes, I'm the medical director of the Center for Pain Relief, which is a large multi-specialty practice in Charleston, West Virginia. And I'm a professor anesthesiology at the West Virginia University School of Medicine, and I have been practicing in the field of pain medicine for over 20 years at this point.

I did my medical school at West Virginia University School of Medicine, did my residencies at the University of Virginia with a primary specialty of anesthesia, and then did a clinical subspecialty of pain management fellowship there under Dr. John Robinson at the University of the Virginia. And since that time I have been practicing in Charleston, West Virginia as a private practitioner and also affiliated with the university.

Q. And can you describe in a little bit more detail your daily practice, the types of patients you see?

A. Yes, we're a group of physicians, nurse practitioners and physician assistants. We treat chronic pain from cancer, so for example, bone metastases and things like that. We also treat non-cancer patients, neuropathy, failed back surgery syndrome, spinal disorders, things of those natures, shingles.

So really a multiplicity of things we treat.

We do medical management, including medication, all the way up to more advanced therapy such as implantable devices such as spinal cord stimulation systems and intrathecal pumps, which are pumps that go in the spinal fluid for chronic pain. We also do many procedures such ablation where we heat nerves and things of that nature.

Q. How many patients do you see in an average day?

A. I personally see an average of about 30 or 40 patients. I see about 40 patients in a day from 7:30 until 4:30. But at the same time my nurse practitioners see patients in the same clinics. So we see about 200 or so patients personally a week, but our current practice is about 500 patients a week under my supervision.

Q. And in your 20-plus years of practicing medicine, have prescribed opioids as part of that practice?

A. Yes, opioids is a part --

THE COURT: I'm not quite hearing you. If you could -- I don't know what to do.

MS. CRUZ: I'll speak louder. Is that better?

THE COURT: That's better, thank you.

Q. So I'll repeat the question.

In your 20-plus years of practicing medicine, have you prescribed opioids as part of that practice?

A. We do prescribe opioids as one of things we do for folks.

Certainly it's part of the algorithm. We prefer non-opioids when possible, but opioids are necessary in some patients to give them relief.

Q. And can you just briefly describe what types of -- what opioids that you use in your practice?

A. Well, certainly with many patients we use quick acting or immediate release opioids on a PRN basis, so as-needed basis. For example, someone that had a fracture of their spine they may need this medicine briefly for few weeks. After a procedure we may use temporary acting or quick acting medication. So we use medications such as immediate release medications if you have had a fracture or had done a procedure that is painful, but if you develop a chronic problem that hurts every day to an intense level, we go to more long-acting medications to give a chronic maintenance therapy.

Q. And if could you turn to slide 3 of the slides.

MS. CRUZ: Your Honor, we marked these as DX 8000, just to be clear for the record.

THE COURT: That's fine.

Q. Have you served as an editor for any industry journals as part of your career?

A. Yes. One of the things I have enjoyed doing is editing articles in the field of pain medicine. I'm the associate editor of the Journal of Neuromodulation. I'm also the editor on board of Pain Medicine, Pain Practice, and Pain Physician.

So those have been part of my professional activity.

I've also been involved in various professional organizations educating physicians in the United States and other countries. These include the American Society of Anesthesiology, which is a 45,000 member group that I chaired for almost four years in the pain division. And the ASA looks at appropriate use of pain therapies.

Also I'm the president elect of the International Neuromodulation Society. And what that is, that's a society that deals with implants in the body, the brain, the spine, the periphery, and research around those issues not just for pain but things like Parkinson's and other disease states, spinal cord injury.

I also chair the Interventional Pain Committee, the American Academy of Pain Medicine, and serve on the board of the American Society of Interventional Pain Physicians, which is also involved in making decisions of policy on opioids. I'm also the Medicare Advisory Committee member for my part of the country in the area of pain medicine.

Q. And in your work as an editor of the various journals and the organizations that you just referred to, do you regularly discuss pain medicine and the use of opioids to treat pain with other practicing physicians?

A. Yes, I do. I just came back last week from the American Academy of Pain Medicine annual meeting where I spoke. A week

before last I was at the Australian Pain Society. And in each of those settings we often discuss the proper algorithm: Should we go with an opioid or another therapy? What's the best opioid?

So I have a pretty good discussion with physicians around the United States about their current practices. Also I have been involved in the State of West Virginia with the governor's oversight task force for opioid abuse and diversion. And so we get to see all the data an abuse and addiction in our state and many other states as we share information with other states and those areas of opioid abuse and diversion.

MS. CRUZ: Your Honor, we would like to offer Dr. Deer as an expert in pain medicine, the treatment of chronic pain, and the use of opioid medications to treat pain.

THE COURT: Fine.

Q. So moving to slide 4, you were retained by the defendants in this case. Can you just give a brief summary of what you were asked to do, and then we can dive into the details on the subsequent.

A. Well, I was retained for my clinical expertise in this area, and I was asked to look at how a clinician such as myself would use the Ranbaxy and Roxane products and compare those uses to method claims in '122 and '216 and respond to Dr. Fassihi's report about those issues.

THE COURT: I'm not understanding you. Take it easy,

a little louder. I am not understanding what you're saying right now.

THE WITNESS: Okay. I will start over on this section.

A. I was asked to look at -- using my clinical experience, how the medications involved in this case from the companies Roxane and Ranbaxy, how they would be used clinically and how that compares to the method claims in the patents '122 and '216. And then I was asked to also look at Opana ER, the particular Endo product, and other treatments and how they figure into our field of treating chronic pain as a specialty.

THE COURT: Okay.

Q. And if we could move to slide 5.

And you had referred to the '122 and '216 patent earlier. Is it okay if we refer to those either by '122 and '216 or the Endo patents?

A. Yes.

Q. And do you have a general understanding of what those patents relate to?

A. Yes, those are patents relating to oxymorphone extended release.

Q. And we also have the '060 patent listed here on the right side of this slide. Do you have a general understanding of what that patent relates to?

A. Yes, that relates to the crush resistant formulation of

oxymorphone extended release.

Q. And given the tasks you identified earlier, did you reach any conclusions?

A. I did reach conclusions about these patents.

Q. And if you could turn to slide 6.

Did you prepare -- is this a summary of the various things that you concluded after reviewing the materials?

A. Yes, this is a summary split into two parts. The first part was that Ranbaxy and Roxane, the products do not meet the requirements of the method claims that are in contention here today in '122 and '216.

The second part deals with the clinical perspective relating to the items listed there, which we'll cover in more detail as we go through my opinions.

Q. So let's turn to that first issue.

THE COURT: Let me look at this for another minute.

Go ahead.

Q. If we could turn to slide 7. And then is this a summary of some of the limitations and the method claims that you reviewed and formed an opinion as to?

A. Yes, these are a summary of some of the claim requirements that I felt were not met by Ranbaxy and Roxane based on some points described previously.

Q. And could you briefly go over these limitations, and then as we go further through the presentation we can describe them

in more detail?

A. Yes, certainly I will go through the points and get into more detail in a little bit. No single person or actor will perform all the requirements of the method claim.

And we're going to focus on three areas. I heard in the past we talked about administration under fed versus fasting conditions and what that means to the patient. Providing and administering the dosage form, what providing means versus administering. And then detection of blood plasma levels the metabolite and oxymorphone compound itself. So we're going to look more closely at those three areas under the claim requirements of the patents in question.

THE COURT: Now why do you introduce the slide by this statement: No single person or actor will perform all of the requirements/steps of the method claims?

THE WITNESS: It's been my understanding from counsel that the method claim legally requires the same actor or person provide and administered dosage form, the same person both provide and administer based on the claim. So that's been the legal explanation that's come to my understanding as part of the method claim.

MS. CRUZ: Your Honor, maybe I can help clarify that.

THE COURT: Okay.

MS. CRUZ: With respect to infringement, normally when you have direct infringement you have one person perform all

the steps. What we're talking about here -- and we'll show you the method claims as we move on, but we're talking about method claims which plaintiffs don't allege any of the defendants infringed directly, or at least the ones we're talking about here, that it's an indirect infringement. So as part of the burden of proof, plaintiffs need to show that each of these limitations is met. And we'll go through them in context, which will probably be more helpful.

And so part of what we need to look at also in this indirect infringement analysis is whether defendants provide any instruction to people taking the pills, the drug, to meet any of these instructions or limitations. So what we're trying to do here from the clinical perspective is figure out if someone follows Ranbaxy's or Roxane's product directions, who was doing what with relation to the various claim limitations.

Does that help, your Honor?

Q. Maybe we can move on.

And you're not a lawyer, Dr. Deer, is that correct?

A. No, ma'am. I have no legal training whatsoever. I'm a clinician and I practice medicine.

Q. And you reviewed portions of Dr. Fassihi's opinion that Ranbaxy and Roxane infringed certain of the method claims of the '122 and '216?

A. I did review that part.

Q. And do you agree with those opinions?

A. I do not.
Q. And we'll go through and explain that in a little bit more detail.
So if you could turn to slide 8. And this was just getting back to the point I made earlier about instructions. Did you look at the product labels and look at the instructions they provide?
A. So the product label -- when you apply to FDA for approval of use of a medication, you give them a proposed label. And I have been involved with the FDA for years on different medications and devices. So you give them a proposed label. And in that label you instruct how someone -- you give the physician instructions how to prescribe the medication that would be within the safety boundaries of the FDA. So I did review the label of Ranbaxy and Roxane's products and the instructions in the proposed labeling and how it relates to the method claims.
Q. And if you could -- maybe what we could do is dive into the claims and maybe provide more context here.
If we could turn to slide 9. And this is -- on the top we have claim 20 of the '122 patent. Do you see that?
A. I do see that.
Q. And did you review the entire claim as part of your analysis?
A. I did review this entire claim as part of the analysis of

this case.
Q. And is there a relevant portion that you would like to discuss?
A. Yes, it's underlined here starting with oxymorphone area under the curve is no more than 20 percent higher when the composition is administered to the subject under fed as compared to fasted conditions.
Q. And is it okay if we refer to that as the fed versus fasted limitation to try and make things a little easier here?
A. That's normally how I would refer to it.
Q. And if you turn to slide 10, you had also addressed some of the claims in the '216 patent, and can you show here on claim 40 and 42 which portions of those claims were relevant to your analysis?
A. Again here looking at the underlined portions it talks about the area under the curve fed versus fasting conditions. Also it look looks the detectable blood plasma levels of both the drug oxymorphone as well as metabolite 6-hydroxy oxymorphone. So these are two of the things in the claim listed in patent '216.
Q. And if you look at both of these claims, they refer back to claim 38. Do you see that?
A. I do see that.
Q. If we turn to the next slide. Slide 8 -- sorry, slide 11 has claim 38 of the '216 patent on the screen here. Could you

describe, with respect to claim 38, which portions of the claim were relevant to your analysis?

A. Yes, I think this is an important part of the claim on '216 patent. Looking at claim 38, the first part underlined is providing a solid oral dosage. That's the providing step in the method claim. The DEA, Drug Enforcement Agency, really monitors how these drugs are provided. So you can't just provide this drug, it has to go through the federal enforcement process. And so there's providing physicians write a prescription and pharmacies provide the medication based on federal law for controlled substances. This is a level II, which is a highly controlled substance.

And then it's administered in a single dose, dosage form, to the subject, which I will call a patient personally, clinically speaking. And administering means actually giving the drug to person. So that is usually self-administered by a patient if it's an oral pill, as opposed to an injection of something that I would give, which I would be both providing and administering it at that point.

THE COURT: I don't understand what issue this testimony is directed to.

MS. CRUZ: Your Honor, these are claims that are asserted by plaintiffs. And so these are -- the limitations we're going over are limitations that the defendants don't -- we feel that plaintiffs haven't proven that defendants meet

these limitations or these pieces of the claim. And so we're introducing them here and then we'll go into a look at what a doctor or a patient would do according to Ranbaxy and Roxane's labels and how that matches up with the claims.

THE COURT: Look, my memory of our pretrial work was that as far as infringement is concerned, it was conceded by the defense that a substantial part of the claims at issue the defense did, their products did -- I'm putting it crudely. But there was a limited issue or issues which were in contest, I thought, on infringement. We were going to limit the proof to what is in contest. I haven't heard anything from this witness about that.

MS. CRUZ: Maybe I can provide a little context for your Honor. Part of the issue is that Dr. Deer is going out of order, so normally plaintiffs would have already provided their contentions with respect to these limitations. And we are only discussing the limitations that are in dispute.

THE COURT: What is he testifying about that relates to what is in dispute?

MS. CRUZ: He's going to testify -- and this was part of the stipulation that we entered into earlier today that Mr. Rhoad mentioned that defendants dispute that any one person has or will directly infringe the methods of patents '122 and '216, which are the claims we're going over, or that any defendant has or will indirectly infringe.

THE COURT: Is that a stipulation? Where is that?

MS. CRUZ: Your Honor, in the stipulation it's item two.

THE COURT: We apparently left ours downstairs.

MR. BLACK: I'm sure we can get another copy.

It's a stipulation admitting infringement, and we can't find it.

Here we go.

THE COURT: Let me look at this a minute.

I am sorry to say I didn't look at this very carefully. It's meaningless to me. The three so-called exceptions to what is conceded, I have no understanding of what that language means at all, not at all.

MS. CRUZ: Perhaps I could help clarify that. Earlier when Mr. Rhoad was up here and he highlighted just a portion of the asserted claims and asked Dr. Fassihi about those claims, he mentioned that there were multiple claims that he didn't highlight, and those claims still had issues in dispute between the parties.

THE COURT: It does not help me at all to list numbers of claims. I need to know what issues, factually not numbers of -- lists of numbers of claims.

MS. CRUZ: If we could turn back to slide 7. So if we look at the bullet points here, your Honor, the administration under fed as compared to fasted conditions, that is one of the

limitations that's in dispute between the parties.

THE COURT: That's right. In other words, the way I remember it is that one thing that is in dispute is whether there's an infringement with respect to the percentage, I guess I can't recite it.

MS. CRUZ: It relates to two terms, that AUC or area under the curve, as well as C max was the other term with respect to fed versus fasted conditions.

But with respect to what we're talking about with Dr. Deer, it's even a little bit more simple because we're talking about method claims. And so it's whether or not -- the issue is whether or not Ranbaxy and Roxane instructed someone to take the drug under fed as compared to fasted conditions. And we will show through Dr. Deer that our labels do not actually provide instructions for patient to take it under fed and fasted conditions and then compare those AUC and C max numbers.

THE COURT: Well, let's have the testimony. It's not at all clear to me what all this -- what you mean by what you are saying, but --

MR. BLACK: Your Honor, may I try for a moment?

THE COURT: What?

MR. BLACK: May I speak for a moment?

THE COURT: Yeah.

MR. BLACK: The issue comes down to this: You heard

testimony from Dr. Fassihi how in the development process tests are run with patients who have -- who are fasting and patients who have food in their stomach to determine whether there's a difference in blood levels between whether you have eaten or not, and that's the food effect. And that's the kind of test they do in pharmaceutical development to see whether a drug, when administered to a patient, whether it makes a difference whether there is food in the stomach or not. And that's all very nicely and in great detail described in the patent how that's done.

The issue they're raising on infringement, and I'm not even sure if it involves all the defendants, because he's only here talking for two of the defendants, I believe what his testimony is is that as a medical doctor reading the claims that he believes that a patient has to do one of these clinical studies.

MS. CRUZ: Your Honor, if I could respond to that. What we're looking at is method claims, and the method of treating pain. And one of the elements of that claim is whether or not you have administration under fed as compared to fasted conditions with respect to the controlled release oxymorphone tablet.

What Dr. Deer is here to do is just to provide the factual basis to show that as a physician reading the product label, the instructions that are provided with these products,

there is no instruction to say that the controlled release oxymorphone is administered under fed as compared to fasted conditions.

THE COURT: Okay, let's go ahead with the testimony.

MS. CRUZ: Why don't we move to slide 14.

And so on the left side of this slide we have just compiled all of the fed versus fasted limitations that are part of the method claims just to orient your Honor. And then what we could do now is just look at these labels that we have been talking about, and perhaps that will help. The witness and your Honor, you have a binder there with various exhibits, and if we could put this up on the screen it's DTX 3542.

BY MS. CRUZ:

Q. Doctor, could you generally describe what this document is?

A. Yes, this is the labeling document for oxymorphone extended release tablets from Ranbaxy.

Q. Can you also look at tab 3523.

A. Yes, I have that before me. This is the labeling instructions for oxymorphone hydrochloride extended release tablets from Ranbaxy as well.

Q. And finally just the third label, just to orient ourselves DTX 3563, can you take a look at that and tell me what that one is?

A. Yes, this is the labeling instructions for oxymorphone hydrochloride extended release tablets from Roxane.

Q. And if you could turn back to our slides DTX 8000, slide 15, do you see there that there's excerpts from the various product labels that we just looked at?
A. Yes, these are excerpts from the labels I mentioned a moment ago looking at the fed versus fasted state.
Q. And what do these instructions provide -- tell you about how a patient would take the extended release oxymorphone tablets with respect to food?
A. I think the important thing is clinically we instruct patients to take this medication on an empty stomach, so at least an hour before they would eat or two hours after they eat. So we would never instruct someone to take this under fed condition. So this is how we talk to patients when we give them instructions about medication, particularly this medication, for all three of these labels, which is what we do daily when we talk to patients.
Q. If you could turn back to slide 14.
THE COURT: So you never instruct them to take it under fed conditions, is that right?
THE WITNESS: No, sir, we never instruct them to do that, it's always under unfed conditions.
Q. If we look at slide 14, after looking at the label seeing that, you never instruct anyone to take it under fed conditions, how does that relate to the fed versus fasted claims that we have here on the slide?

A. Well, again, if the patient follows our instructions and that of Ranbaxy and Roxane's labeling, then they would not take it under fed conditions, and certainly we would not conduct any pharmacokinetic testing on a patient. So we wouldn't ask a patent to do a study because we don't the dose this medication based on that. The availability of 20 percent or 30 percent clinically is not consequential. The consequential part is does it help the pain or not, are there side effects or not?

THE COURT: I'm not understanding what you are saying.

THE WITNESS: Clinically we consider we only instruct it under fasting conditions only, and then we make our decisions about the dosing and things based on the patient's response not on pharmacokinetics testing, we don't instruct any pharmacokinetic blood testing to make decisions.

THE COURT: Any what?

THE WITNESS: Any blood testing. We don't test their blood to see if they're responding properly. We don't draw plasma levels or C maxes or areas under the curve or anything like that clinically.

THE COURT: Does the patent do that?

THE WITNESS: The patent does do that?

So then these --

THE COURT: The patent does what?

THE WITNESS: The patent involves the method of doing those things, drawing serum levels and things of that nature.

Clinically we don't do any of those things based on the instructions of Roxane and Ranbaxy.

THE COURT: Go a little slower. The patent does what?

THE WITNESS: So the method claim in the patent instructions to fed and fasting dosing and then draw blood levels and look at the differences in the method claims. We clinically don't do that. We instruct people to take it only fasting, and we don't require any blood drawing to determine the dosing.

THE COURT: Are you saying that the patent says that a patient is supposed to do both and then they're supposed to compare? Is the patient supposed to do that, according to you?

THE WITNESS: No, we recommend that clinically -- I'm speaking from a clinical standpoint, we don't recommend that they do that. And the labeling of these two --

THE COURT: What does the patent do?

THE WITNESS: The method claim of the patent involves testing the blood and also giving it under fed state.

THE COURT: Under what?

THE WITNESS: The patent claim has a method of giving the drug under a fasting state and then a fed state and then comparing the two based on blood draws.

THE COURT: Comparing the two. To find out how much drug gets into the blood?

THE WITNESS: That's right. But clinically treating

patients based on the labels that we talked about a moment ago, we don't recommend that.

THE COURT: But you're saying that the patent involves a patient and taking the patient and having the patient try the drug out before the meal and after the meal, is that what you're saying that the patent says should be done?

THE WITNESS: The patent method claim has them taking the pill before the meal, but some other time taking it with the meal, in the fed state. That's what the patent method claim recommends or has a method claim.

THE COURT: In the treatment of a patient, they would -- or under the patent they could take it before eating, right?

THE WITNESS: So the patent method claim has before eating as one of the times.

THE COURT: What do you mean by the method claim?

THE WITNESS: I'm not a lawyer, but the method claim is the part of the patent that instructs the method of the patent.

THE COURT: Okay, fine. And you're saying that the method claim, it's the method of treating a patient, right?

THE WITNESS: That's right.

THE COURT: And the patient can take the drug before eating, right?

THE WITNESS: That's correct.

THE COURT: And after eating, right?

THE WITNESS: No. Well, on a full stomach.

THE COURT: With a full stomach.

THE WITNESS: Yes.

THE COURT: As a remember the patent, it says that the difference of how much drug gets into the bloodstream is less than 20 percent, isn't that what the patent says?

THE WITNESS: It looks at different percentages. I'm not sure the number, but looks at different percentages comparing the fed to fasting. And they draw blood to figure that out, they draw blood from the subject.

THE COURT: All right.

THE WITNESS: Clinically -- my testimony is that clinically if you follow the labels of these two labels that we just talked about a moment ago, Ranbaxy and Roxane, you would not do that. The FDA, which controls this, would have you give the medicine only in the fasting patient and not to draw any blood to test any levels.

THE COURT: Okay. All right. Fine.

BY MS. CRUZ:

Q. Then why don't we move on to the next limitation that is in dispute between the parties, and if we could turn to slide 16 to look at that next limitation.

So looking at claim 38, there is the term "administering" in that claim, and in other claims it appears

as "administered" or "administration," and did you, in your review of the claims, come to an understanding along with your expertise of what that term means?

A. I did. To administer a drug means to physically deliver the composition into the body of the patient. So to administer a drug is to actually have a drug go into your body, whether that be by pill form or some other method, in this case by pill form.

Q. And if could you turn to slide 17.

A. Yes.

Q. Could you describe -- earlier you mentioned in your testimony that claim 38 has one step of providing and a second step of administering. Can you explain that in a little more detail?

A. Yes, providing a drug like this to a patient involves a prescription being written by the doctor, and a pharmacist delivering or providing the medication to the patient. So that is regulated by the DEA, because it's a controlled substance. So to be a provider of opioids you have to have a DEA license and the pharmacy has to have a DEA license. That means you're providing an opioid, which is different than administering, which means you're taking it. So in this case the patient would take the pill, as opposed to an injection in your vein in a hospital where I could both provide and administer to the patient. So there's a difference between the two.

THE COURT: Wait, wait. I'm not sure I get what you're saying. Go over that again.

THE WITNESS: So --

THE COURT: I want to understand what you're saying.

THE WITNESS: Absolutely. So I will try to explain that again, and if I don't do a good job, I will do it again.

So claim 38 has two separate steps, and that's the whole point medically speaking. And again, I'm not giving a legal opinion, I'm giving a medical opinion. One is providing a solid oral pill, so a pill, that's step one, providing. And in the United States, to provide a level II opioid, which this is, all of these manufacturers, these are level II opioids, that's the highest level, control level, level II, with the DEA, the Drug Enforcement Agency. You have to have a physician write it based on the controlled substance laws and his or her state and the federal law, and then you have to have a pharmacist with a license dispense the drug or provide the drug to patient. That's step one, it takes a physician and a pharmacist to do step one.

Step two is administering. And to administer this drug, the patient would have to take the pill. So this is called a sel-administered drug because it's oral.

So the point is I was asked clinically is this two different steps, and the answer is it certainly is with this type of drug because it's a heavily controlled substance.

THE COURT: How does this relate to issues in our case?

THE WITNESS: I would defer that to legal counsel on both sides, but what I understand is there is a question of one person can do the whole thing, can one person both provide and take the medicine. And providing, to me, means two -- at least three people are involved in this process, a physician, a pharmacy, and a patient. I was asked if that could be with one person or need to be more than one. Clinically speaking it has to be three. The legal issues --

THE COURT: To deal with what is in the patent --

THE WITNESS: Yes.

THE COURT: -- requires three persons?

THE WITNESS: The patent method claim, certainly I could let the lawyers speak to that, but the clinical question for me was is this one step, one person do this whole thing, and clinically speaking in America it takes three people to do this step.

THE COURT: Before the patient can take the pill, right?

THE WITNESS: Well, it takes two people before the patient can take the pill, the doctor and the pharmacy, because they have to be licensed to do so by the federal government. And then the patient administers this pill to themself, as opposed to IV injection. For example, chemotherapy, the same

doctor may provide it and administer it, that could be one step if you have a chemotherapy drug. But this is very different. This is a pill prescribed --

THE COURT: What does this have to do --

MS. CRUZ: If I may, your Honor, legally it matters whether these two steps are done by the same or separate people as a matter of patent law. And so what he's saying is factually in a practical aspect it's separate actors. So if one actor legally does not perform all the steps, then defendants don't infringe this claim or the claims depending from this claim. So that's the issue in dispute between us and plaintiffs.

THE COURT: Say that again.

MS. CRUZ: Sure. So legally it matters whether these two steps, the providing and the administering, are done by the same or separate people. And some of the case law says "actor," but I will use the term "people."

And what Dr. Deer is saying is that factually in practice it's separate actors that are performing these two steps, the physician and the pharmacist on one hand and then also the patient. And so if one actor doesn't perform all of these steps, then defendants don't infringe this claim or the claims that depend from this claim.

THE COURT: This claim being?

MS. CRUZ: Claim 38. And claim -- there's several

dependent claims that are asserted that include these limitations. So for example, claims 40 and 42 of the '216 patent.

THE COURT: Where is it in the patent that talks about how many people have to be involved?

MS. CRUZ: It's a combination of the case law as well as the patent itself. So this --

THE COURT: Where in the patent does it say this?

MS. CRUZ: It's part of the legal framework in determining whether or not this patent claim, claim 38, which is up on the screen, whether or not that is infringed by a single person.

Plaintiffs are alleging that the defendants induced or contribute to other people infringing these claims, and there is case law that says that if we're in that context, a single person needs to perform the steps that are in the claim. And so our point here through Dr. Deer is that it's not a single person performing these steps.

THE COURT: And what persons do perform the steps?

MS. CRUZ: So for the providing step it would be the physician or the pharmacist, and with respect to the administering it would be the patient.

THE COURT: And you're saying that the patent just means that one person is involved? Is that what you're saying?

MS. CRUZ: What I'm saying is that the patent lists

the steps, so there is step A, providing, step B, administering.

THE COURT: Where does it say that?

MS. CRUZ: If you look at claim 38, it's on the screen there, and if you look at step A of --

THE COURT: Just a minute. Claim 38. Which patent?

MS. CRUZ: It's the '216 patent, your Honor, it's PTX 5, if that helps.

THE COURT: So the '216 patent, right?

MS. CRUZ: Correct.

THE COURT: And claim 38.

MS. CRUZ: 38. It's in column 29 of the patent.

THE COURT: Right.

MS. CRUZ: And it's towards the bottom left-hand corner, claim 38. And you will see part A, and it says providing a solid oral dosage form.

(Continued on next page)

THE COURT: Just a minute. I see that.

Q. And then the claim continues on, actually, to the next column, and then there is a part B. Do you see there at the top of column 30?

THE COURT: Right.

MS. CRUZ: And step B says "administering a single dose of the dosage form," so administering the solid oral dosage form, which in this case is the controlled release oxymorphone.

THE COURT: What is the point that you are making?

MS. CRUZ: The point is that the patent lists these two different steps and to infringe the claim, you have a two-part thing. The steps have to be performed, but the law requires that all of the steps be performed by one person or one actor, and our point here --

THE COURT: Wait a minute.

What did you say claim 38 means on the subject you are talking about?

MS. CRUZ: So claim 38, if you take a step back, it is a method claim for treating pain.

THE COURT: That's right.

MS. CRUZ: So step A of that method is providing a solid oral dosage form. And then I'm not going to go into the rest of that part of the claim, because it is not relevant to what we are talking about right now. And step B requires

administering that solid oral dosage form to the subject or to the patient.

THE COURT: I am sorry to say I just don't understand any other way to do it. "Providing," to me, means manufacturing, whatever is needed to make the pill. And I assume that, whether you are a plaintiff or a defendant here, if you are trying to provide the pill, the pill has to be manufactured. It doesn't come out of nature. Whether it is plaintiffs' side or the defense side, the pill has to be manufactured. And then obviously you don't keep it in a desk drawer, so it is given to somebody to take. How else could it be?

MS. CRUZ: What's relevant here, your Honor --

THE COURT: How else possibly could it be?

MR. CLEMENT: Your Honor, if I may, Alan Clement on behalf of Roxane, so the issue here is there has to be direct infringement of the claim. Under the recent Supreme Court case, and this is spelled out in our pretrial brief, proof of direct infringement can only occur when all of the steps of a method claim are performed by one actor. That is the way the Supreme Court has said method claims have to be looked at when determining infringement. This only applies to these claims, 40 and 42, which depend from 38. This defense doesn't apply to the other claims in this case, but the way this claim is written it is just fatally defective. Because, as your Honor

said, "providing" means manufacturing, "administering" means the patient ingesting the drug, and since that necessarily requires two actors, it cannot be infringed. And, as Dr. Deer has been testifying, he is confirming that, that providing is done by other actors than the --

THE COURT: Are you saying the Supreme Court says it has to be one actor?

MR. CLEMENT: Yes, I am, your Honor.

THE COURT: In other words, the same person has to manufacture it? Has the Supreme Court held that? The same person has to manufacture the pill and give it to a patient?

MR. CLEMENT: What the Supreme Court held in the *Limelight* case is that all of the steps --

THE COURT: I am asking you a more specific question.

MR. CLEMENT: I understand that, and I think, under the holding of the Supreme Court, that is how that would be interpreted if they were presented with this specific claim. The case before the Supreme Court dealt with another multistep method claim, and they said since one actor did not perform all the steps, even though multiple actors did perform --

THE COURT: I think the Supreme Court case is talking about something much different than what we are talking about.

MR. CLEMENT: I think the Supreme Court was very clear in its holding and it has been followed in other cases, and it is set forth on page 22 of our pretrial brief --

THE COURT: We are not going to go on endlessly, but why don't you go ahead and let's complete this examination and we will get back to the legal issues later, of course.

MR. CLEMENT: Thank you, your Honor.

THE COURT: All right.

Go ahead.

MS. CRUZ: Why don't we switch gears to secondary considerations at this point.

THE COURT: All right.

MS. CRUZ: And, your Honor, this is an analysis that's relevant to all three patents, and what Dr. Deer will be responding to is just some various assertions plaintiffs have made regarding Opana ER and the marketplace, and we can turn to those now.

Q. On slide 21, does this show the various areas of assertions that plaintiffs have made that you were looking at from a clinical perspective?

A. Yes, this summarizes the clinical opinions I made based on those areas of interest and secondary considerations.

Q. And in forming your opinions, are there areas of expertise that you drew upon?

A. Yes. I looked at my own clinical practice for 21 years; looked at my work around the country with other physicians, other societies, and policy-making areas; my work in the state legislature in West Virginia, looking at new legislation to

curb drug abuse; and also my experience of my colleagues as well in the area of commercial success.

Q. If we could turn to slide 22, and if you could describe briefly your statement here that there were adequate treatment options available prior to introduction of Opana ER and Opana ER CRF.

A. Yes.

Your Honor, I am going to talk about three areas here clinically.

The first is in 2006, when Opana ER was first approved, I am going to look at what else we had available clinically at that time to treat similar patients. So that's the long-acting opioid issue.

Then I am going to look at some of the benefits you may see with this medication being attributable to the compound itself, oxymorphone, not to the sustained-release version of that or the extended-release version.

And then, lastly, and sadly, I am going to look at how the crush-resistent formulation really has done nothing to change drug abuse in America, which is what we see on a daily basis around the U.S. So those are the three areas I am going to use my clinical --

THE COURT: Has the crush-resistent feature done something to reduce the use of this kind of pill?

THE WITNESS: No, sir, I believe has not, and the FDA

agrees with me on that so far.

THE COURT: Oh, okay.

Do drug addicts just crush it?

THE WITNESS: No, the drug addicts tend to take more pills. So if they took one before and crushed it, now they can take three or they can dissolve it and take it in the dissolved state. So they don't have to crush it to abuse it. These folks are very savvy.

THE COURT: How do they abuse it again?

THE WITNESS: For example, instead of maybe take one pill, they may take two pills or three pills or four pills. They may dissolve it and do other things with it, such as shoot it in their vein or drink it. So they can do a lot of things with it besides crush it, unfortunately. So this has really done, in my opinion, nothing to stem the abuse of the medication.

BY MS. CRUZ:

Q. If we could turn to slide 23. If you could explain this slide and how it relates to the marketplace when Opana ER was first introduced in 2006.

A. So, in 2006, when Opana ER was first introduced to physicians in America to use, the question is, was there a large need for this medication? At that time we had other drugs listed here that gave either 12-hour or 24-hour dosing, or in the case of the now patch, the Duragesic patch, up to

every three days you put a patch on your body. We also had methadone, which has a long half-life, and we had a drug not listed here, Tramadol Extended Release which now is controlled.

So we had many agents at that time that were sustained-release agents. So this wasn't a drug that we were all clamoring for, if you will. There was no long felt need to bring this to the marketplace. It was another opioid option that was brought to our clinical practice.

Q. Looking at the dosing schedule column that's on this chart, can you explain that in a little bit more detail?

A. Yes. There are two groups of opioids. There is the short-acting opioids, which last three or four hours, so that's things like Tylox or Percocet, I think Lortab, where you take it every four hours or so when you break your leg or you have some new injury. Those drugs are not good long-term because you have to take them so often it becomes a real problem.

So there are long-acting drugs where you give them every 8 to 24 hours, 12 hours, listed here, labeled by the FDA, that last much longer. So we had a lot of options in 2006, all the options listed here plus another option called Tramadol Extended Released. So we had at least eight options at that time for patients who had chronic pain and didn't want to take a pill every three or four hours.

Q. Just so we have it clear in the record, can you just describe which long-acting opioids are listed here on the

chart?
A. Yes, MS Contin, Oramorph, Kadian, Avinza, all of which are forms of morphine; OxyContin, which is oxycodone; Duragesic which is a patch; Fentanyl; methadone, which is a drug that is long-acting, given to drug addicts for abuse, but also given for pain in some cases; and then, not listed here at the time, as I thought of it, going through the slide, was Tramadol Extended Release which is another mu-receptor drug.
Q. Even beyond, this is just a list of opioids. At the time Opana ER was introduced in 2006, there were also non-opioid treatments available. Is that true?
A. That's true. We tried to avoid opioids when possible using physical therapy, injections, neurostimulators, and also pumps that infuse medication in the spinal fluid, intrathecal drug delivery systems in some cases. So these are the opioids that were available, but in some cases we can control pain without that. A good example is kyphoplasty, where we could cement into a broken bone in the spine rather than put them on pills. So there are other things we can do other than opioids in 2006 and today.
Q. And if we can turn to slide 24, you had also mentioned that there were various factors that affect your prescribing decisions.
A. Yes. I think my prescribing decisions are similar to other doctors. We look at the effectiveness of treatment. Does it

help the patient? That's number one.

Number two, we look at cost. For example, if a drug is helpful, but the patient can't afford a large copay and they can't get the medication, then it is not of much value.

Side effects, and then the patient's previous experience with opioids, we wouldn't give someone on a long-acting opioid if they have never had a short-acting opioid because they would be naive to the medication and could have major issues.

We look at the route of administration, such as through the skin versus through the mouth versus through the spinal fluid; the dosing schedule, long-acting versus short-acting; and then, lastly, we look at the risk of abuse, which is a problem in America right now, and drug diversion, which is when they sell their medication to someone else, which is another problem. So we look at all these factors when we prescribe a medication.

THE COURT: We will take a recess, please.

THE WITNESS: Yes, sir.

(Recess)

THE COURT: Go ahead, please.

MS. CRUZ: Thank you, your Honor.

We are going to move into some assertions, just due to Dr. Deer being out of order in the case that you will hear about from plaintiffs further on in the case, so I just wanted

to make a couple of factual points that we disagree with plaintiffs on.

THE COURT: Go ahead.

BY MS. CRUZ:

Q. Looking at slide 25, you had mentioned earlier that some of the benefits are attributable -- some of the benefits plaintiffs have mentioned are attributable to the active ingredient oxymorphone. Can you explain that in a little bit more detail?

A. Yes. So oxymorphone has been used clinically in the past, in the 1950s and '60s. It was used by IV and by suppository. It was used in other countries at other times. And in recent years, since 2006, it has been available commercially in the United States. One of the issues at hand is whether or not it is the oxymorphone itself, the compound, or the formulation involved in the patent we have been discussing this afternoon. So those are the issues that I was asked to look at.

THE COURT: Say that again, please.

THE WITNESS: So the issues are, some of the things that will be discussed about oxymorphone, which is the active drug that we are discussing, is it the oxymorphone compound or is it the formulation the patent involves? The patent involves an extended-release version of oxymorphone, so it is limited to extended-release oxymorphone. But the active ingredient is the compound oxymorphone. So it was available before. It wasn't

invented in this patent. It was already available as a compound. So that's what I have been asked to look at; is it the oxymorphone or is it the invention that became clinically available in 2006?

THE COURT: The issue being?

THE WITNESS: The issue being is there something special about the extended-release version involved in these patents or some of the things we are going to discuss in this slide, as you see in this slide on the board. Is it related to the compound, the active ingredient, which is not what this patent is about.

THE COURT: Go ahead.

BY MS. CRUZ:

Q. Looking, first, at your first bullet point, talking about metabolism of oxymorphone, can you just briefly describe the process of metabolism of oxymorphone with respect to the CYP2D6 that's mentioned here?

A. Yes. There is an enzyme in the body that breaks down oxymorphone to its metabolites including hydroxy-oxymorphone. And some people have a gene that isn't very good for that, so they are what we call a poor metabolizer. So if you give them oxymorphone, they really won't process it. That is directly related to the compound and has nothing to do with the extended-release version of it. It is the drug itself, not the issue in the patent. So that's the issue with the metabolism

that is related directly to oxymorphone compound.

So in some cases, there are genetic tests available where you can determine if someone has the right enzymes; but, clinically, speaking as a doctor who takes care of these folks, that isn't a relevant issue because no one pays for that genetic testing. For example, Medicare doesn't pay for genetic testing of that enzyme system, so you couldn't, even if you had the test available, you could not use that test to determine if someone is a metabolizer of this compound.

Q. And there is also, we will hear talk about CYP354 enzyme as well. Does that also interact directly with the oxymorphone? Can you explain that?

A. Yes. The issue there is if you take oxymorphone with other drugs, there can be some interactions. Again, they can be complete interaction or partial interactions. But in all those cases, it is the oxymorphone compound that is important, not this extended-release version of it that is debated in these patent litigation cases.

And then, lastly, the side effects of opioids, they all have side effects. Opana ER has side effects. Morphine has side effects. Oxycodone has side effects. So these side effects are seen in all patients who take opioids to some degree, and Opana ER is just another one of those opioids.

So that you can see euphoria with Opana ER just like you can see euphoria with morphine. You can see nausea, things

of that nature, with Opana ER as you can with oxycodone. So it is a molecule in Opana ER that causes side effects, not the formulation debated in these patents.

So the points of those first three issues really go back to the action of the molecule which was available before the patents, it was invented before the patents.

Opioid rotation is the last issue clinically. Opioid rotation is a process where someone is on morphine for six months and it quits working for them. They develop tolerance. You rotate them to Fentanyl, because their body hasn't seen that drug before, and then over six months they get tolerant to that drug. Then you can go to oxycodone. Then they get tolerant to that drug, and you go to methadone and you go back to morphine or you go to oxymorphone. So "opioid rotation" means you change the drug based upon someone getting tolerant, where it doesn't work as well, or getting side effects.

That isn't done in patients who are doing well, though. You would keep them on the same drug they have been on. That is also a factor of the molecule of oxymorphone, not anything to do with the patents of the extended-release version of it.

So those are the points I wanted to clinically make about the molecule versus the compound, extended-release medication.

Q. If we can turn to slide 27, I just want to expand a little

bit on the opioid rotation point you mentioned.
A. Yes. I have 27 before me.
Q. Can you explain how it is that it is the molecule that is relevant to opioid rotation in providing a different response in the patient?
A. Yes. So in your spinal fluid in your brain, you have receptors that bind opioid, so there are different receptors. There is mu, which is involved in the pain response, and then there are other receptors, sigma, kappa, gamma, other receptors. So if you give someone a compound such as morphine, it will bind in a certain fashion to those receptors. If, over time, they don't do as well as they were doing, you can go to Fentanyl, for example, and that may bind differently to those receptors. And oxymorphone, the active ingredient of that drug, would do the same thing; it would bind differently.

So the whole point of opioid rotation is based on the receptors in the spinal fluid and the spinal cord and the brain seeing different things it hasn't seen before, so that it may respond better if someone gets tolerant. So opioid rotation could be helpful in certain patients because they develop tolerance to a medication. Other patients may be on the same drug for ten years and never develop tolerance and keep their dose really low, and their receptors aren't prone to tolerance.

So that's the issues at hand with opioid rotation.
Q. If we could actually go back to slide 26, I just wanted to

touch on a little bit more on the metabolism that you mentioned. With respect to CYP2D6 and CYP3A4, I believe you testified that those are both enzymes involved in metabolism of oxymorphone?

A. Well, certainly one is -- they are both involved in the metabolism and in the pathways in the body, that's correct.

Q. Is CYP2D6 known to be a problem with respect to OxyContin?

A. Oxycodone can be one of those drugs which has difficulty with that enzyme system, that's correct.

Q. And actually what we have up on the screen here is, if we can look at the top selection, that is a section of the drug-drug interaction section of the Opana Immediate Release product label, and it is DTX 2071, and we also on the screen have an excerpt on the bottom from the extended release, Opana ER product label, and that is taken from DTX 0879.

So if you look at these two sections, from the immediate-release and the extended-release product, does that have any bearing on your opinion that it is an interaction of the oxymorphone active ingredient with the CYP354 enzyme?

A. Yes. I believe this is very important in that the FDA has not stipulated a difference between the two, and certainly here in the labeling, the immediate-release product label, as approved by the FDA, used the data from Opana ER on this issue so the FDA felt that they were the same, which would suggest the molecule is the important factor here. And so I think

that's consistent with FDA labeling policies of drugs such as this.

Q. Then if we could move forward to slide 28?

A. Yes, I have 28 before me.

Q. I believe you have made all these points, but I am not sure that you had drawn out point three, if you could explain that point.

A. Yes. As I have said earlier, I do not believe the crush-resistent formulation has really stopped abuse of Opana. Also the FDA has ruled currently, in my understanding, that their risk-versus-benefit ratio favors keeping the label the same and not allowing --

THE COURT: Favors what?

THE WITNESS: The FDA, when they were asked to change the labeling for abuse deterrence of the crush-resistant formulation said, no, that there was no evidence that the benefit was great enough to change the label for diversion or abuse. So they would not -- they found insufficient evidence to allow doctors to be told about the abuse deterrence. So when you come talk to a physician about this medication, if you work for a company, you are not allowed to tell us it changes abuse, because there is no evidence that the FDA found credible to show that. Currently speaking, I have seen no evidence of that either, nor have I seen evidence, as I have traveled the country and talked to other physicians.

And then the last point is that we have made some headway in drug abuse in America, fortunately, in the last few years. I think that's from several factors. And Opana ER crush-resistent formulation or the other companies that have similar things has not been the reason why. We have had new legislation, new laws around the country making it more difficult for these pill mills who give medications without justification. We have had education of physicians about proper prescribing and how they should do routine office visits and monitoring of the patient.

So I think the other factors that contribute to reduction, which has been shown in multiple areas, including the State of Washington, which recently showed a major reduction in prescribing of opioids, has been based on physician education and legislation more than anything else. So I would certainly hope we continue to collaborate with physicians and government to help continue to strengthen laws and safety around these issues.

Q. In your experience, is there a stigma for patients associated with any particular opioids?

A. Well, there certainly has been a stigma with opioids. For example, when I first started practicing in West Virginia 21 years ago, people would come in and they would say, Don't give my grandmother morphine for her broken bone in her spine because it is morphine. Give her something else. So they knew

that word "morphine."

Over time, oxycodone had a stigma with it; and then as oxymorphone became more common, and we started to see it mentioned in newspapers and news report, it is began to get a stigma in some cases as well.

So it seems that every time a new medication comes out to the availability of doctors, we see an initial uptick in the reputation of the new medication. But, unfortunately, anything that can be abused, we see that over time also become stigmatized.

So I do believe there is a stigma for opioids in general in noncancer patients, and that's something that we see clinically from our patients and their families.

Q. So turning to unexpected results, if you could turn to slide 30.

A. Yes, ma'am, I have slide 30 before me.

Q. On this slide you mention that certain benefits are common to all controlled-release formulations. Can you describe what you mean by that?

A. Well, I have been using controlled-release formulations for many years. So we expect certain things that are not unexpected. If you give someone a controlled-release formulation, you expect them to take medicine less often. That's the whole point. If you give someone a medicine they take once or twice a day or every three days in the case of a

patch, you expect improved compliance because they don't have to remember to take a patch every day or take a pill six times a day. If they don't have to wake up in the middle of the night to take a medicine, then their sleep improves generally. So that's an expected result of a controlled-release medication. And you expect in some cases there will be fewer side effects. That's not always the case. And, in fact, even with controlled release, all opioids have side effects. But it wouldn't be unexpected if they had less side effects.

Q. And if we can move to slide 31, you had mentioned benefits that were attributable to the active ingredients, and we have already talked about the drug-drug interactions, but if you could explain your point on urine monitoring.

A. Well, a few years ago it was very difficult to monitor certain drugs in the urine, and that's been part of the legislation that has been passed around the country is if someone is on a chronic opioid, you should see them in the office and do urine drug screening.

What we find now is that we have very high complex urine screening tests, so we can measure the urine monitoring and the compliance with all these medications -- morphine, oxycodone, oxymorphone and the metabolites.

I think if there is any benefit of oxymorphone in urine, it would be from the active ingredient, not the drugs in the patents, but I think but with the high complexity urine

screening we are seeing less benefit from that point overall anyway.

Q. Maybe for the court reporter you could just slow down a little bit.

A. No problem.

Q. So turning now to slide 32, and it looks -- let's discuss some of the prescribing decisions and factors that may be raised that do not impact your prescribing decisions.

A. Well, we talked earlier about the main factors and decided what prescription to write for someone in pain. We talked about safety, effectiveness, cost, availability, other disease states, experience with opioids. All those things are important.

What doesn't impact physicians in my opinion and, again, speaking to physicians around the country and in my practice, they have little or no expectations about drug formulations and the bioavailability of the compound. They rarely ever consider this and certainly isn't a part of their clinical thinking or training.

I have medical students with me all the time in my rotation, and certainly it is not something we teach in the medical school as a component of this factor in most cases. And then dissolution testing doesn't impact our prescribing at all. In fact, I would think most physicians wouldn't even understand what dissolution testing means. So the

bioavailability and the dissolution testing aren't important factors in prescribing. It is those other things that I mentioned earlier that are important.

Q. Turning to slide 33, if we could move to the commercial success topic.

A. So, I was asked my clinical opinion of whether or not this drug Opana ER was clinically, commercially a success clinically, so I had a few thoughts on that based on my experience.

One is, Endo has been very aggressive in marketing this medication. Physician brochures mailed to your office and offices that allow representatives, representatives talking to physicians about prescribing this, they have had online Internet coupons for patients to get the medication. So they have been very aggressive. I don't think there is anything wrong with that. That's just a way companies present their medication to people. So I don't have a criticism of that in any fashion.

Despite that, Opana ER has not become a first-line treatment for most clinicians, including myself, for several factors which I mentioned earlier. In my practice it has been a third- or fourth-line therapy, and I think that's pretty consistent with my colleagues as I have traveled the country.

Q. Can you describe what your first- and second-tier drugs would be with respect to opioids?

A. Our first tier is try to avoid long-term opioids. We try to other things, such as procedures or physical therapy or drugs like Gabapentin, which is a non-opioid. If those things aren't successful and we go to opioid, we try to keep opioids on a limited basis, on an as-needed basis initially. If that is successful, we would stay with that over time.

But there are cases where an extended-release medication is needed and is clinically appropriate. In those cases, morphine, which is MS Contin or one of the other morphine extended-release drugs, has been one of our first choices. Second line of therapy has been Duragesic or other Fentanyl patch prescribing areas. OxyContin, certainly in low-risk patients for abuse, has been a third-line choice in some patients, although certainly has had a history of diversion. And Opana ER, to me, is in a similar group, with OxyContin, as a third- or fourth-line option in those patients. So certainly it is acceptable clinically. It is certainly a drug that is certainly reasonable to prescribe. It is just not a first-line therapy in clinical practice for myself or most other physicians that practice pain medicine.

Q. Just to clarify, your opinions on commercial success, those are based on your clinical perspective. You are not an economist, is that correct?

A. No. I don't have any opinion on whether or not it is a profitable drug or things of that nature. So I would defer

that to people with that expertise, certainly not me.
Q. And turning, more specifically, to the Opana ER CRF version, if we can go to slide 34.
A. Yes, ma'am, I have the slide before me.
Q. This one deals with some commercial success points with respect specifically to the crush-resistent formulation. Can you elaborate on these points?
A. Well, I was asked if I felt Opana ER CRF, which is the crush-resistent formulation, had any significant demand from physicians, and I would tell you that my discussion with physicians, both locally and around the country, including family practice doctors, is most of them don't know this even exists. As we said earlier, the FDA has not allowed that to be marketed in that fashion, so most physicians still write for Opana ER as their primary drug when they give this medication. In fact, when I write for this medication, that's what I have written for as well.

I was surprised to learn that it is not substituted for generic, because I don't keep track of what's generic and of that nature over time. So apparently it is not substitutable. So if you write Opana ER currently, then they get the brand product, which, again if they can afford that, I have no problem with that. It's just not well understood by physicians.

So the point is that I think the crush-resistent

formulation hasn't changed the demand because, number one, doctors aren't told that it changes abuse, because it is not allowed to be marketed that way; and, secondly, most physicians, when they write for Opana ER, I don't think they understand the generic substitution for this product versus the brand-necessary product.

Q. If we could turn to the final slide, slide 35, this slide has to do with industry acclaim. I believe you already stated these points, but do these points also apply to whether or not you feel there has been acclaim in the industry for the Opana ER CRF product?

A. Yes. When you go to a meeting, for example, the American Academy of Pain Medicine I mentioned a moment ago, we have another meeting in three weeks of the American Society of Interventional Pain, when something new comes along, there is a lot of chatter among doctors, Have you seen this, have you tried this for your patients? And certainly I have not seen any of that with this medication. That's not to say it is a bad medication in any fashion. It has just not had acclaim in the industry thus far in my opinion.

MS. CRUZ: Your Honor, we have reviewed several documents today with Dr. Deer, and if it is acceptable to the court --

THE COURT: Are you offering them?

MS. CRUZ: Yes.

THE COURT: Received.

MS. CRUZ: Would you mind, for the record, if I could list the DTX and PTX numbers just so it is clear for the record?

THE COURT: It is a waste of time.

MS. CRUZ: DTX 0879 --

THE COURT: Please. You can do that with the court reporter after the session.

MS. CRUZ: Okay. Thank you, your Honor.

THE COURT: Any further questions of this witness?

MS. CRUZ: No further questions.

(Defendants' Exhibits DTX 0879, DTX 2071, DTX 3523, DTX 3542, DTX 3563, DTX 6000 received in evidence)

THE COURT: Is there no cross?

MR. BLACK: Oh, there is cross, your Honor. Yes.

We have a bit of a scheduling issue. We have had a long direct, and I am not sure I am going to be able to get my cross done. I understand that Mr. Deer will be able to come back, not next week, but maybe the following week if we have to.

Is that correct?

THE COURT: Well, do your best. We can even get on the telephone, if necessary.

MR. BLACK: It might not be as exciting, but all right.

CROSS EXAMINATION

BY MR. BLACK:

Q. Dr. Deer, I'm going to start from back to front with your examination.

You basically, I would sum up your testimony -- tell me if it is fair -- that tamper-resistent technology for opiates is no big deal. You don't think it is very important, right?

A. I don't recall saying it that way, sir. What I said was currently there is no evidence that I have seen, either by studies or in my experience, that it has changed abuse potential of the medications, and the FDA has agreed with me on that point so far.

Q. So far.

So you believe that the tamper-resistent technology that's currently available is not adequate, not relevant, not commercially successful?

A. In my hometown there have been recently some teenagers overdose on this substance, so I think it doesn't keep you from taking more than you are supposed to, for taking diverted drugs, for taking dissolved drugs. You can still find ways to abuse this drug and die from it if you take it improperly, and that's what drug addicts do. So I don't think there is any clinical evidence, in studies or definitely not in society, that has changed anything as of yet. If a study is done that

shows that, I would be glad to view that and comment.
Q. You mentioned your hometown. You are from West Virginia, is that correct?
A. That's correct.
Q. My condolences on the basketball game last night. I believe you guys had a tough night.
You said earlier in your testimony that you do some sort of consulting work for the state, are involved in reviewing data relating to opioid abuse, is that right?
A. No. It's not consulting work. It's volunteer work. We have a task force of the Pharmacological Oversight Committee, which I serve on at the appointment of the governor, and we look at things like death from different medications, including heroin, which is not prescribed. The medical examiner is involved in that, the board of pharmacy runs the task force along with the D.A., the state police, and other physicians --
THE COURT: Can I ask you, listen very carefully to his question and limit your answer to his question and that's the way we can make progress.
THE WITNESS: Yes, sir. I will do so. Thank you.
Q. Are you familiar with Patrick Morrissey? Do you know who he is?
A. Patrick Morrissey is the Attorney General, I believe, currently.
Q. Of West Virginia, correct?

A. Yes, sir.
Q. He seems to disagree with you. Do you know that?
A. No, I didn't know that but certainly I would be glad to hear what Mr. Morrissey has to say.
Q. Let's take a look at tab eight of your binder. Do you have a binder up there, white binder?
A. No, I don't. No one gave me one, sir.
Q. Okay. Well that's a problem. We will correct that.
MR. BLACK: Does the court have a binder?
THE DEPUTY CLERK: We are fine. Thank you, Mr. Black.
A. Thank you very much. Which tab was that, sir?
Q. That would be tab eight.
A. Tab eight? Yes, sir.
Q. This is a letter, it is a one-page letter from the National Association of Attorneys General. Do you see that?
A. I do.
Q. It is dated March 11, 2013. It is an unusual letter in that the text of the letter is one page and the signatures run to three pages. Do you see that?
A. I do see that.
Q. It is signed by almost all -- I think 48 -- of the attorneys general of the various states of the United States. Do you see that?
A. I do.
Q. The letter is addressed to the Food and Drug

Administration, specifically to Margaret Hamburg, who was then the head of the FDA. Do you see that?

A. I do.

Q. I want to see whether you agree or disagree with the 48 attorneys general of the United States.

First thing they say is, "Relief from pain is important to millions of individuals who suffer from chronic illness and prescription drugs, such as opioids, have proven useful."

Do you agree with?

A. I think in some patients they are very useful.

Q. They then say, "However, the abuse of prescription drugs is a significant danger and has reached epidemic levels in many of our states."

Do you agree with?

A. I certainly agree with that.

Q. "Against this background, the development of tamper-resistent drugs provides an opportunity."

Do you agree?

A. Certainly an opportunity. I do agree with that.

THE COURT: Wait. Do you agree or disagree?

THE WITNESS: I think it is an opportunity. I would agree with the term it is an opportunity, yes.

Q. "Adding new physical and chemical features to prescription opioids to deter abuse could reduce misuse of these drugs and

its sometimes deadly consequences."

Do you agree?

A. I agree with the word "could reduce," yes.

Q. "These products can be part of a comprehensive approach which should include prevention, interdiction, prosecution, and substance abuse treatment."

Do you agree with that?

A. Certainly not opposed to that in any fashion.

THE COURT: You better just be a tiny bit slower.

MR. BLACK: Okay.

Q. "In our states, nonmedical users are shifting away from the new tamper-resistent formulations to nontamper-resistent formulations of other opioids as well as to illegal drugs."

Do you agree with the 48 attorneys general who signed this letter?

A. Not exactly. That's not what has been showing.

THE COURT: Read that again.

Q. "In our states, nonmedical users are shifting away from the new tamper-resistent formulations to nontamper-resistent formulations of other opioids as well as to illegal drugs."

In other words, once the tamper-resistent products came out, drug abusers shifted from the tamper-resistent to the available nontamper-resistent products, isn't that right?

A. I don't think that's correct, and I can tell you why if you would like.

Q. I just want to know at this point whether you agree with the 48 attorneys general who signed this letter, yes or no? Yes or no, sir.
A. I partially agree because heroin is on the rise, there is no question, in every state, including West Virginia. But a move away from all opioids is also being seen, not just tamper-resistent. So I would agree that that's one of the categories, but certainly I don't think it has anything to do with the tamper-resistent portion of that. But heroin is on the rise terribly right now.
Q. I don't believe I asked you about heroin, but thank you.
A. You said illegal drugs, sir.
Q. "There is great concern in our law enforcement community that many nontamper-resistent products are available for abuse when only a few products have been formulated with tamper resistent features."

Do you agree with that concern or is that not a concern of yours?
A. Well, certainly I know the state police well in West Virginia, and they are concerned about all opioid abuse and diversions, and that would be one of the things they would be concerned with. And this is helpful, so I would tend to agree with that overall.
Q. "As a specific example, we are concerned with the possibility that generic versions of extended-release opioid

prescription drugs and other nontamper-resistent products may reach the market."

Do you agree with that? Do you have that concern?

A. I'm not sure I understand the concern. They are talking about generic tamper-resistent drugs?

Q. "We are talking about generic versions of extended release opioid-resistent drugs, like the generic products in this case."

Right?

A. It appears that's their opinion on this issue. I think we should hopefully reduce the use of all opioids when possible as well as diversions. So I would agree with that as I would any opioid reduction.

Q. So you would agree that generic versions of extended-release opioid prescription drugs and other nontamper-resistent products should not reach the market, correct?

A. No, I wouldn't agree with that. I would say there is no evidence of that so far with tamper-resistent drugs, which makes a difference. So I would agree all opioids should be reduced where appropriate to reduce diversion, so that would be my thought on that. So I can't agree with that as written because I don't think there is any evidence scientifically or clinically it is true.

Q. So you disagree with the opinion of the 48 state attorneys

general of the United States?
A. I doubt there are any physicians among those 48 folks. I am speak clinically, so I have got no political -- in fact, I know Mr. Morrissey invited me to his fundraiser, so I know him fairly well.
Q. Have you made any political contributions to him?
A. I have not. I think I went for free, but he invited me and I did meet with him actually. Seems to be a nice guy.
Q. "We applaud the FDA for expeditiously proposing guidelines establishing clear standards for manufacturers who develop and market tamper- and abuse-resistent opioid products while considering incentives for undertaking the research and development necessary to bring such products to market."
Do you applaud the FDA for putting those guidelines out?
A. They should have guidelines, and that's why they haven't approved yet the language to be marketed, because they haven't shown that based on that study that you are talking about. So, yes, more research should be done. I agree 100 percent that more research is needed to show any effect of this tamper-resistent drug.
Q. Are you aware that the FDA has published guidelines on this issue?
A. I am aware of it.
Q. Have you read them?

A. I don't know if I have or not. I have read a lot of materials. I may have.

THE COURT: I didn't understand the question, please.

MR. BLACK: I will back up, your Honor. I introduced a new thought here.

Q. The FDA, actually, is actually very concerned about the proper methodology for approving drugs with tamper-resistent claims, right?

A. So, I think Janet Woodcock wrote something about these guidelines that I read and reviewed, and I think she is the one that saw the decision so far that the evidence wasn't adequate; and if that be the case, she may have been the one calling for more guidelines and been part of that. So I may have seen it. Under oath, I don't want to say I haven't seen it. I don't recall what it says exactly. I know they called for more expeditious study and money being spent on it.

Q. Right. You know that generally there are FDA guidelines for approving tamper-resistent products but you haven't read the guidelines in preparation for your testimony today, is that right?

A. That's not what I said at all, not even close to what I just said.

Q. Okay. Which one did I get wrong? Are you aware or are you not aware whether there are FDA guidelines? Yes or no.

A. Sir, I said a moment ago I was aware of that. I did read

some materials signed by Dr. Janet Woodcock, I believe was her name, which I can certainly look at if you have, and that may have been part of those guidelines, but I can't recall the exact guidelines currently. I do know they exist. And I would applaud them for creating such a thing, so I would agree with that part of the sentence.

Q. If you take a look at the last sentence of the letter, the conclusion, "Most importantly, we encourage the FDA to assure that generic versions of such products are designed with similar features." Do you see that?

A. I do see that.

Q. Do you agree with at that statement or you disagree with the attorneys general of the United States?

A. Well, again, I am speaking from a clinical standpoint, not a politician's standpoint. But I would say that if that research shows tamper-resistent medications do make a difference, which certainly would be great, that would be something we should try for. Right now there is no clinical evidence that I am aware of that shows that makes a difference in abuse or deterrence, and we are not seeing that in communities.

Q. Let's talk about communities. Let's talk about drug abuse in the path to towing the line. So I heard you testify, and it is certainly the case, that one method of abuse of opioids is to take too many pills, right?

A. That's correct.
Q. And there is a next step along the line, though, which is, if you can do it, crushing the pills and snorting it, correct?
A. That would be a method, yes.
Q. Yes, it would.

And it's a method that many people use in the United States tragically, correct?
A. I think that's true.
Q. It is also a method that is, if the pill can be easily crushed, which unfortunately is preferrable for teenagers, because they are normally going to be afraid and worried about the next step along the line, which is intravenous injection, isn't that right?
A. You know, I haven't seen any studies on that. Most of the teenager abuse we see is taking pills. So I don't think what you said is scientifically correct, and I don't know much about the fear of teenagers using IV drugs.
Q. First step along the road is taking too many pills, right?
A. Again, I'm not a teenage expert on how they abuse drugs. You mentioned teenagers taking too many pills. We have an abuse unit at a local hospital we get a lot of referrals from after they go through rehabilitation to try to treat pain without opioids, and certainly those people do a lot of things. They shoot drugs up. They snort drugs. They take drugs by mouth. They do a lot of things with medication. So I think

that drug addicts find many ways to abuse medication, all of which are unfortunate.
Q. First and easiest thing is, as you testified before, steal some pills and take them and maybe take more than you need to, right?
A. Unfortunately I don't think most of it is theft. I think it is selling on the street or diversion, so I think that's a more common theme we are seeing, rather than thefts.
Q. And if the drug user gets to the next stage and says, you know what, those pills, especially those controlled release pills that last for hours and are designed to have lower blood levels, if they want to get high faster, easiest way to do that is to find a crushable pill, crush it, and snort it, isn't it?
A. I have treated probably 2 to 3,000 people with abuse histories in my career. None of them has ever told me what you just said. So I know you are testifying to that, but certainly my testimony would be, I have never queried that nor have I seen any research or literature on that.
Q. You are not aware that people take pills and crush them and snort opioids to get high?
A. I said earlier people do that as one of the methods, but you keep saying it is the easiest method. I don't think that's true.
Q. Is it easier or harder to take one of the crushable generic tablets that are at issue in this case, crush them up and snort

them than to prepare -- to obtain the necessary tools and prepare IV injection?
A. Again, I don't have a good opinion on that. I would say more people take pills than anything else. People do shoot up drugs all the time, though. We see them in the hospital with phlebitis. But snorting them would be another option in a noncrush-resistent pill. That's the whole theory behind it, and if the study shows that makes a difference, I am certainly not opposed to it.
Q. It's a lot easier to crush up a pill and snort it than it is to prepare it for IV injection, isn't it?
A. I wouldn't think so. They dissolve it in a spoon with some heat, so that would seem pretty easy to do, and we do see IV drug abusers pretty often in consultation, so I don't have any scientific evidence to mirror what you just said, because some people don't really like to snort drugs, but some people do. So is it easier? I don't know. I certainly haven't tried either method. I have seen both patient groups.
Q. And if you are talking about the folks who -- the hardcore drug abusers who dissolve the drug in the spoon and inject it, they, too, have to crush the pill to get the drug so they can put it into the solution to inject, don't they?
A. Well, we are seeing a lot of abuse of Opana right now in that fashion, so how they are able to do that is certainly something I am not an expert in, but they are able to do it.

We see it pretty often.

THE COURT: Look. Can I just interrupt?

The questions are really about your common sense, and that's what I am listening for. In other words, Mr. Black is asking about how one might do a certain thing, and I will have to tell you that I don't find it particularly of interest to hear about the lack of research or the lack of studies and all that. It seems to me that the questions are questions about, as a matter of common sense, common sense of your profession, is this doable or feasible or whatever.

Let's listen to the questions with that in view. He is not asking for a research paper.

THE WITNESS: Yes, your Honor. I appreciate that insight. Thank you very much. Yes, sir.

BY MR. BLACK:

Q. So you would agree, would you not, that in order to get a quick high from one of the opioids at issue in this case, a user could, and many do, crush the pills, which can be done quite easily in most of the formulations in this case, and snort the drug, correct?

A. So I think you used the word "most," and the most common thing we see is people taking more pills than they should.

Q. Right.

A. People do snort the pills sometimes. And you are correct; if you can crush that pill, it is easier to snort.

Q. Thank you.

And also in preparing the drug for injection, a drug abusers will take the pill and grind it up, which they can easily do, and then put it into solution in a spoon, I think you said something about heating it up -- I'm not sure if that's needed, but if you say so -- and then they inject the drug into their body, correct?

A. We do see people who inject all these drugs into their body.

Q. Right. Now, you said there was a lack of scientific evidence on the topic, right?

A. Well, again, I was speaking towards studies but your Honor wanted me to talk more clinically, so that's what I am doing currently.

Q. You are familiar with the history of OxyContin's reformulation, aren't you?

A. I am.

Q. And you know that OxyContin had a crushable pill which was taken off the market and has now been replaced by a tamper resistent pill, correct?

A. I am not sure all of the steps along the way, but I know they have had some issues with the one pill being taken off the market.

Q. And they now have a crush-resistent pill on the market, right?

A. I believe they do. I don't use that as a primary agent of mine.
Q. The FDA gave them approval to call it tamper resistent?
A. I believe that's accurate.
Q. Do you know that the very same technology that's used in the OxyContin pills is used in the Opana pills?
A. I think they both involve a tamper-resistent component.
Q. Right, which came from Grunenthal, right?
A. That's my understanding, yes, sir.
Q. You mentioned lack of data. You are here as a rebuttal witness to Dr. Ross, who is the plaintiffs' expert and had to leave to treat patients, as I know all of you do, and he will come back next week. But your testimony is, in part, in response to Dr. Ross, correct?
A. I believe that's correct, yes, sir.
Q. And you reviewed Dr. Ross's report, right?
A. I did.
Q. Would you look at tab 5 of your binder. We have a copy there of Dr. Ross's report. I want to give you an opportunity to respond to some of his statements, since he is testifying later in the case and we are out of order.
Dr. Ross, if you look at paragraph 2, he is a clinical instructor in anesthesia at Harvard Medical School and an associate professor of anesthesia at Harvard Medical School.
Are you aware of that?

A. I am, that's correct.
Q. You would agree that he is a pain management specialist like yourself?
A. That's correct.
Q. Dr. Ross, in his report, said that there is data that he has reviewed relating to the issue of Opana ER's superiority over the original version, correct?
A. Can you point me to the part of the report where he says that, sir?
Q. Why don't you take a look at page 52. Excuse me, paragraph 52 at the bottom of page 18.
A. Okay.
Q. Dr. Ross, in his report, which you are here to testify in rebuttal to, said that epidemiological studies have demonstrated that crush resistance of Opana ER CRF has reduced abuse of Opana ER CRF by snorting compared to the original formulation of Opana ER. And it goes over to page 19, and then he cites an Endo document, Endo production, a report, research report.

Do you see that?

A. I do see that.
Q. It didn't look like, in your expert report that we -- where we got the documents that you reviewed, that you even bothered to read that report. Have you read it?
A. Well, I certainly work with many journals --

THE COURT: The question is did you read the particular report?

THE WITNESS: No, sir. I don't recall reading that report.

Q. He then wrote, "Notably, despite lower prescription volumes, the rate of abuse of generic oxymorphone ER is higher than Opana ER CRF with snorting as the most common route of administration among abusers of generic oxymorphone."

You didn't read that section of the report, did you?

A. I don't recall reading Endo documents, but -- Endo-based studies.

Q. He then wrote, in paragraph 53, "Qualitative data have also shown that abusers prefer generic oxymorphone for abuse compared to Opana ER CRF. In online discussion boards, individuals indicated that the generic crush-up, just like the old Opana ER formula, and can be easily snorted. The brand are trash. And that considering, as a poster said, that the generics are available, don't waste your time with tamperproof." That was also in that report which you didn't read.

A. I don't recall reading this Endo document, so if someone has those materials I would certainly be glad to review it, again. But I don't recall. I know it was produced by Endo.

Q. Were you curious at all about which generic tablets he might be referring to there that are preferred to Opana ER CRF?

A. Again, I don't recall seeing the document, so I would have to see the document to comment on that further, I think.
Q. We can accommodate you. Take a look at tab 7, PTX 376, page 62.
A. Yes, sir, I am there.
Q. Take a look where it says "many authors" in the middle?
A. Which page are you on, sir?
Q. 62 of 65. Are you there?
A. No.
Q. The pages are numbered several ways because of the production. Do you see? Oh, 62 of 85.
A. Yes, sir, I am there. "Selection" --
Q. Actually go up one paragraph. "During Q2 2014, authors participating in discussion on the monitored Web sites often expressed negative opinions of reformulated Opana ER due to its tamper-resistent properties. For example, one individual wrote that reformulated Opana ER tablets were 'by far the hardiest opiate in pill form you will find' while another simply stated 'yeah, I' curse word 'hate Opana ER. If you get lucky enough to get IRs' -- that's immediate release -- 'they are amazing.' Yet another individual indicated that it was useless to attempt snorting the product as it just gels up in contact.
Do you see that?
A. I do see that, yes, sir.
Q. It says many, "Authors participating in discussion during

Q2 2014 suggested seeking out generic oxymorphone ER products in place of the brand Opana ER, indicating that the generics were more effective and desirable for recreational use. One author wrote that use of reformulated Opana ER was a waste and stated that not only is it hard to break down for sniffing, it doesn't work when taken orally either."

Do you see that?

A. I do see it.

Q. "The author went on to strongly suggest asking for the generics when you fill your prescription. Several authors also made similar statements."

Here is the next one. It says, "Did you get brand or generics? The Actavis generics crush up just like the old formula and can be easily snorted. The name brand are trash."

On the next couple of pages, there are actual quotes taken off the Web sites.

Are you aware that folks who abuse drugs go on Web sites and swap information with them.

A. Well, it looks like Endo has gone to Web sites, your client, and picked things off the Web that said these things. I don't get in these chat rooms, so I am sure there are many chat rooms that would say whatever you would like. So the credibility of this is pretty limited, in my opinion, based on coming from the people who make the drug.

Q. This is actually a survey produced by an outside expert,

but since you haven't reviewed it, I really only have one other comment on it, which is, that this comment is about the Actavis generics crushing up like the old formula. Are you aware when the Actavis generics came on the market?

A. I don't understand your question.

Q. Do you know that the Actavis generics came on the market during the course of this case?

A. I am not sure of the exact date.

Q. Did you know than Endo sought a preliminary injunction to prevent that from happening, but failed; and, as a result, these generics from Actavis went on the market before we could have our trial here?

A. No, I don't know that.

MR. BLACK: Your Honor, this might be a good point to break. I am not going to finish cross and I am sure they have redirect.

THE COURT: Let's break.

What about this witness?

MR. BLACK: I don't control him, obviously. Someone else will have to speak to that.

MR. ZIMMERMAN: Your Honor, we will confer about it and find a way to get it done with plaintiffs.

THE COURT: I'm sure you will.

Okay. We will break now. I am going to try to start earlier in the day so we have fuller days, so we will start at

10:30 Tuesday.

MR. BLACK: Thank you, your Honor.

THE COURT: We are recessed until 10:30 Tuesday morning. All right.

(Adjourned until Tuesday, March 31, 2015, at 10:30 a.m.)

INDEX OF EXAMINATION

DEFENDANT EXHIBITS